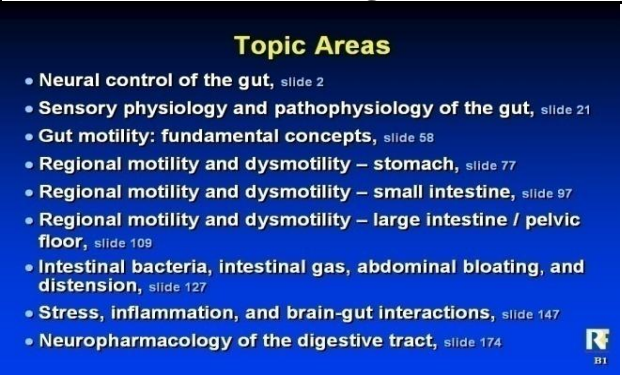
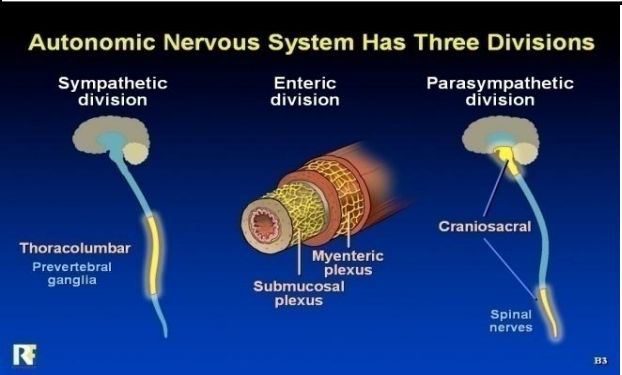
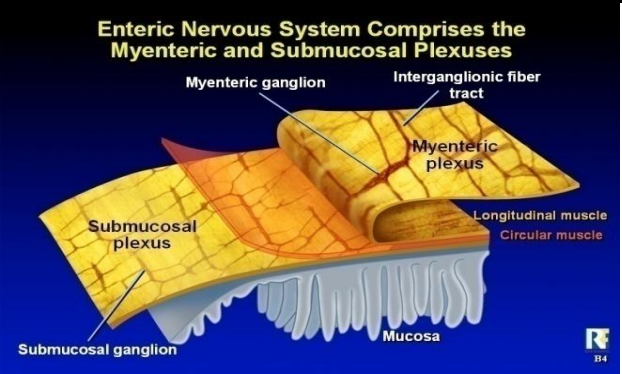


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Slide Number	Slide Title	Slide Image
B1	Topic Areas	<p>Topic Areas</p> <ul style="list-style-type: none"> • Neural control of the gut, slide 2 • Sensory physiology and pathophysiology of the gut, slide 21 • Gut motility: fundamental concepts, slide 58 • Regional motility and dysmotility – stomach, slide 77 • Regional motility and dysmotility – small intestine, slide 97 • Regional motility and dysmotility – large intestine / pelvic floor, slide 109 • Intestinal bacteria, intestinal gas, abdominal bloating, and distension, slide 127 • Stress, inflammation, and brain-gut interactions, slide 147 • Neuropharmacology of the digestive tract, slide 174 
B2	Section Title: Neural Control of the Gut	
B3	Autonomic Nervous System Has Three Divisions	<p>Autonomic Nervous System Has Three Divisions</p> 
B4	Enteric Nervous System Comprises the Myenteric and Submucosal Plexuses	<p>Enteric Nervous System Comprises the Myenteric and Submucosal Plexuses</p> 

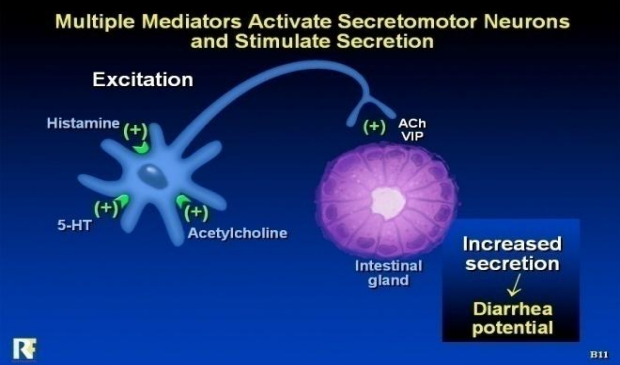
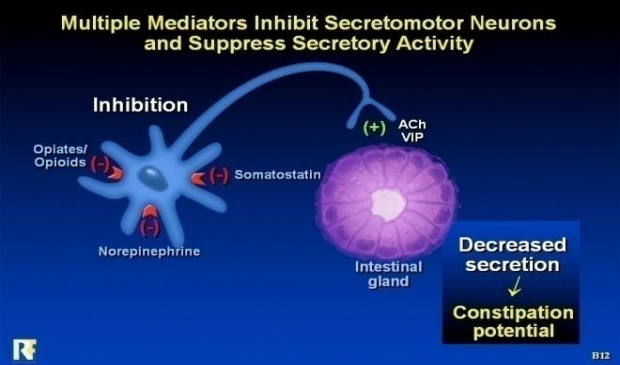
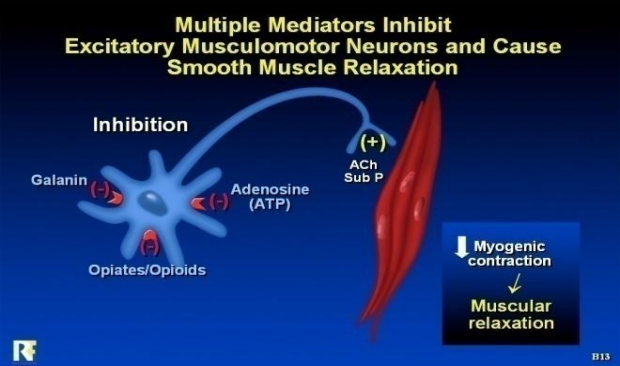
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<p>B5</p>	<p>Enteric Nervous System (ENS): The “Brain-In-The-Gut” Concept</p>	<p>Enteric Nervous System (ENS): The “Brain-In-The-Gut” Concept</p> <p>Brain-like functions of ENS</p> <ul style="list-style-type: none"> • Program library • Feedback control • Reflexes • Information processing <p>ENS “Brain-in-the Gut”</p> <p>R B5</p>
<p>B6</p>	<p>Microcircuits of the ENS Are Formed by Synaptic Connections Between Sensory Neurons, Motor Neurons, and Interneurons</p>	<p>Microcircuits of the ENS Are Formed by Synaptic Connections Between Sensory Neurons, Interneurons, and Motor Neurons</p> <p>Sensory neurons</p> <p>Enteric nervous system</p> <p>Interneurons</p> <ul style="list-style-type: none"> • Program library • Feedback control • Reflexes • Information processing <p>Motor neurons</p> <ul style="list-style-type: none"> • Muscle • Secretory epithelium • Blood vessels <ul style="list-style-type: none"> • Motility patterns • Secretory patterns • Circulatory patterns <p>Gut behavior</p> <p>R B6</p>
<p>B7</p>	<p>Bidirectional Communication Occurs Between the ENS and the CNS</p>	<p>Bidirectional Communication Occurs Between the ENS and the CNS</p> <p>Sensory neurons</p> <p>Enteric nervous system</p> <p>Central nervous system</p> <p>Interneurons</p> <ul style="list-style-type: none"> • Program library • Feedback control • Reflexes • Information processing <p>Motor neurons</p> <ul style="list-style-type: none"> • Muscle • Secretory epithelium • Blood vessels <ul style="list-style-type: none"> • Motility patterns • Secretory patterns • Circulatory patterns <p>Gut behavior</p> <p>R B7</p>

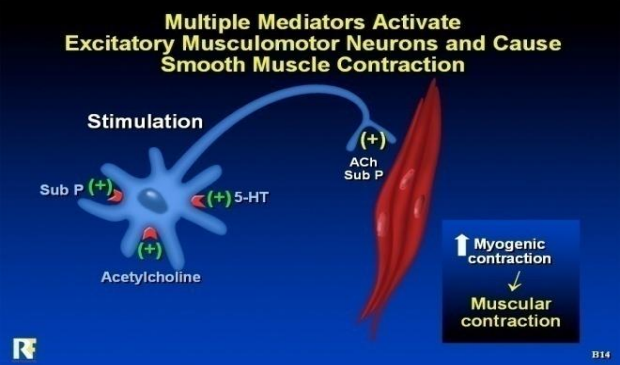
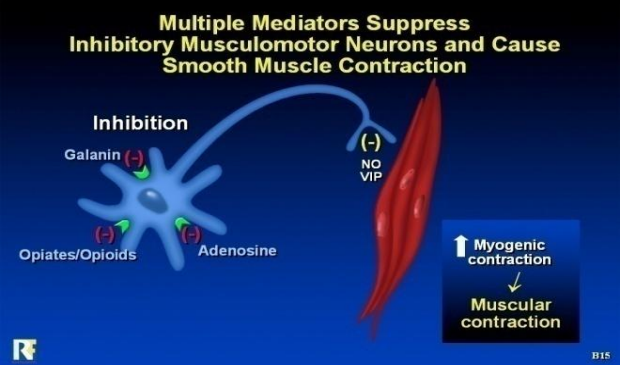
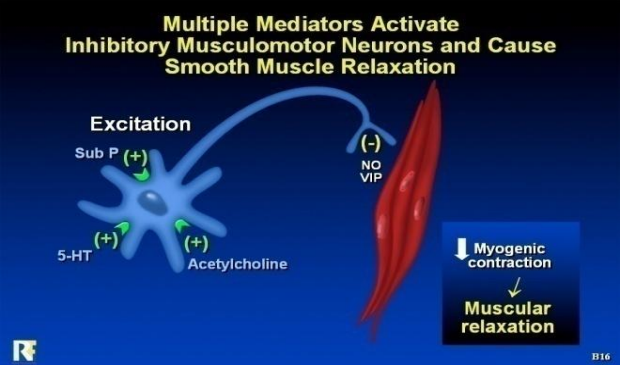
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<p>B8</p>	<p>Three Main Types of Chemical Signaling Occur in the Enteric Nervous System</p>	<p>Three Main Types of Chemical Signaling Occur in the Enteric Nervous System</p> <p>Neuron to Neuron Synaptic Transmission</p> <p>Endocrine Cells Enteroendocrine Cell</p> <p>Paracrine Cells Enterochromaffin Cell Enteric Mast Cell</p> <p>Examples</p> <ul style="list-style-type: none"> • Acetylcholine • 5-HT • Substance P • Norepinephrine • CCK • Gastrin • 5-HT • Histamine • Inflammatory cytokines <p>R</p>
<p>B9</p>	<p>Sensory Neurons in the Enteric Nervous System</p>	<p>Sensory Neurons in the Enteric Nervous System</p> <p>Dorsal vagal complex Nodose ganglion cell Vagal afferent</p> <p>Output to central pathways</p> <p>Direction of transmission</p> <p>Detection</p> <p>Channels / receptors</p> <p>Spinal afferent Dorsal spinal ganglion cell</p> <p>R</p>
<p>B10</p>	<p>Motor Neurons in the Enteric Nervous System</p>	<p>Motor Neurons in the Enteric Nervous System</p> <p>Secretion</p> <p>Secretomotor neuron (+) ACh VIP Intestinal gland</p> <p>Motility</p> <p>Inhibitory musculomotor neuron (-) NO VIP Intestinal smooth muscle</p> <p>Excitatory musculomotor neuron (+) ACh Sub P Intestinal smooth muscle</p> <p>R</p>

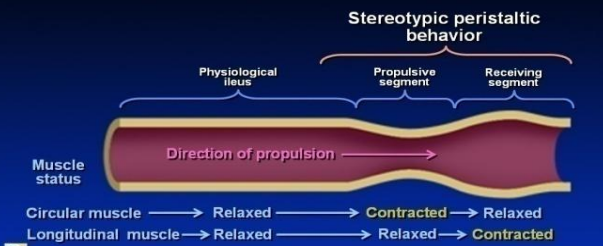
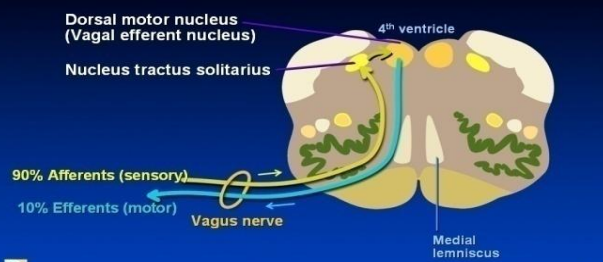
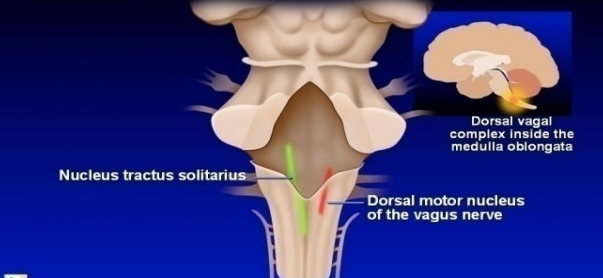
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B11	Multiple Mediators Activate Secretomotor Neurons And Stimulate Secretion	 <p>Multiple Mediators Activate Secretomotor Neurons and Stimulate Secretion</p> <p>Excitation</p> <p>Histamine (+) 5-HT (+) Acetylcholine (+)</p> <p>ACh VIP (+)</p> <p>Intestinal gland</p> <p>Increased secretion ↓ Diarrhea potential</p> <p>R</p> <p>B11</p>
B12	Multiple Mediators Inhibit Secretomotor Neurons And Suppress Secretory Activity	 <p>Multiple Mediators Inhibit Secretomotor Neurons and Suppress Secretory Activity</p> <p>Inhibition</p> <p>Opiates/Opioids (-) Somatostatin (-)</p> <p>Norepinephrine (-)</p> <p>ACh VIP (+)</p> <p>Intestinal gland</p> <p>Decreased secretion ↓ Constipation potential</p> <p>R</p> <p>B12</p>
B13	Multiple Mediators Inhibit Excitatory Musculomotor Neurons and Cause Smooth Muscle Relaxation	 <p>Multiple Mediators Inhibit Excitatory Musculomotor Neurons and Cause Smooth Muscle Relaxation</p> <p>Inhibition</p> <p>Galanin (-) Opiates/Opioids (-)</p> <p>Adenosine (ATP) (-)</p> <p>ACh Sub P (+)</p> <p>Myogenic contraction ↓ Muscular relaxation</p> <p>R</p> <p>B13</p>

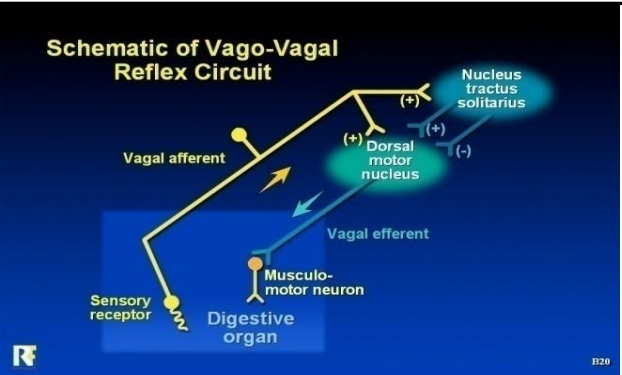
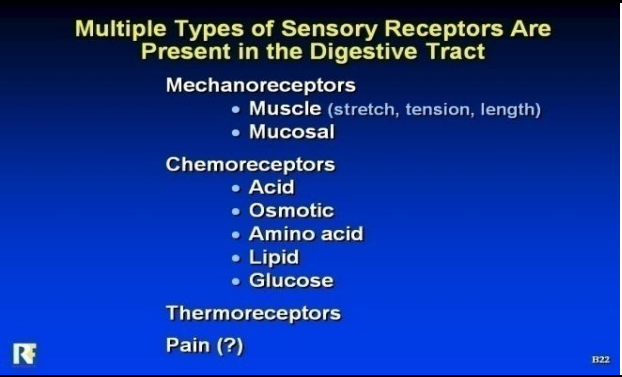
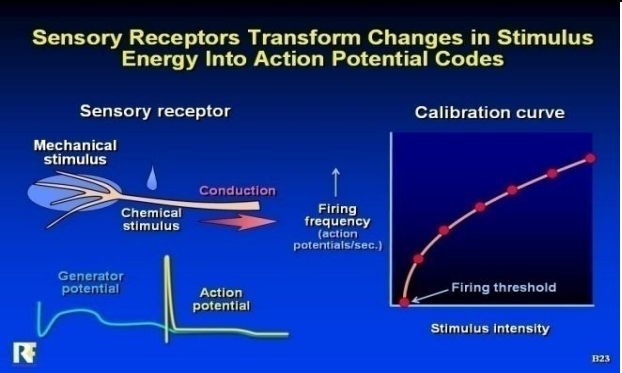
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B14	Multiple Mediators Activate Excitatory Musculomotor Neurons and Cause Smooth Muscle Contraction	 <p>Multiple Mediators Activate Excitatory Musculomotor Neurons and Cause Smooth Muscle Contraction</p> <p>Stimulation</p> <p>Sub P (+) 5-HT (+) Acetylcholine (+)</p> <p>ACh (+) Sub P (+)</p> <p>↑ Myogenic contraction ↓ Muscular contraction</p> <p>B14</p>
B15	Multiple Mediators Suppress Inhibitory Musculomotor Neurons and Cause Smooth Muscle Contraction	 <p>Multiple Mediators Suppress Inhibitory Musculomotor Neurons and Cause Smooth Muscle Contraction</p> <p>Inhibition</p> <p>Galanin (-) Opiates/Opioids (-) Adenosine (-)</p> <p>NO (-) VIP (-)</p> <p>↑ Myogenic contraction ↓ Muscular contraction</p> <p>B15</p>
B16	Multiple Mediators Activate Inhibitory Musculomotor Neurons and Cause Smooth Muscle Relaxation	 <p>Multiple Mediators Activate Inhibitory Musculomotor Neurons and Cause Smooth Muscle Relaxation</p> <p>Excitation</p> <p>Sub P (+) 5-HT (+) Acetylcholine (+)</p> <p>NO (-) VIP (-)</p> <p>↓ Myogenic contraction ↓ Muscular relaxation</p> <p>B16</p>

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<p>B17</p>	<p>Neural Control of Longitudinal and Circular Muscles Forms Propulsive and Receiving Segments During Peristaltic Propulsion</p>	<p>Neural Control of Longitudinal and Circular Muscles Forms Propulsive and Receiving Segments During Peristaltic Propulsion</p>  <p>Stereotypic peristaltic behavior</p> <p>Physiological ileus</p> <p>Propulsive segment Receiving segment</p> <p>Direction of propulsion</p> <p>Muscle status</p> <p>Circular muscle → Relaxed → Contracted → Relaxed</p> <p>Longitudinal muscle → Relaxed → Relaxed → Contracted</p> <p>R B17</p>
<p>B18</p>	<p>Vagus Nerves: Mixed Afferent and Efferent</p>	<p>Vagus Nerves: Mixed Afferent and Efferent</p>  <p>Dorsal motor nucleus (Vagal efferent nucleus)</p> <p>Nucleus tractus solitarius</p> <p>4th ventricle</p> <p>90% Afferents (sensory)</p> <p>10% Efferents (motor)</p> <p>Vagus nerve</p> <p>Medial lemniscus</p> <p>R B18</p>
<p>B19</p>	<p>Dorsal Vagal Complex in Medulla Oblongata Contains the Dorsal Motor Nucleus and the Nucleus Tractus Solitarius</p>	<p>Dorsal Vagal Complex in Medulla Oblongata Contains the Dorsal Motor Nucleus and the Nucleus Tractus Solitarius</p>  <p>Nucleus tractus solitarius</p> <p>Dorsal motor nucleus of the vagus nerve</p> <p>Dorsal vagal complex inside the medulla oblongata</p> <p>R B19</p>

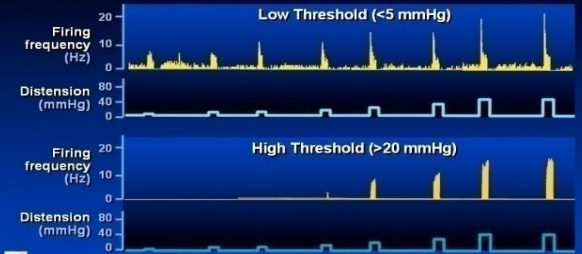
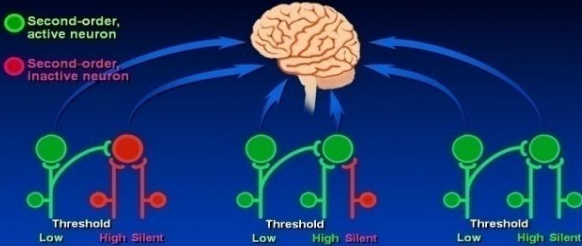
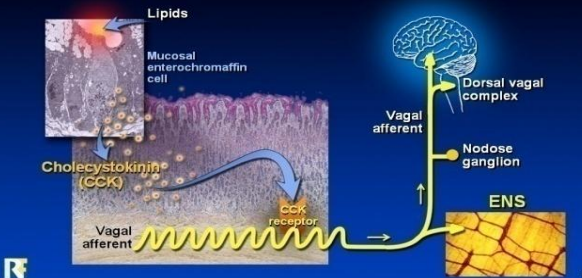
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<p>B20</p>	<p>Schematic of Vago-Vagal Reflex Circuit</p>	 <p>Schematic of Vago-Vagal Reflex Circuit</p> <p>The diagram illustrates the neural pathway of the vago-vagal reflex. A sensory receptor in the digestive organ sends a signal via a vagal afferent to the dorsal motor nucleus in the brainstem. The dorsal motor nucleus then sends a signal via a vagal efferent to a musculo-motor neuron in the digestive organ. The nucleus tractus solitarius is also shown, with excitatory (+) connections to the dorsal motor nucleus and inhibitory (-) connections to the vagal efferent pathway.</p> <p>R B20</p>
<p>B21</p>	<p>Section Title: Sensory Physiology and Pathophysiology of the Gut</p>	<p></p>
<p>B22</p>	<p>Multiple Types of Sensory Receptors Are Present in the Digestive Tract</p>	 <p>Multiple Types of Sensory Receptors Are Present in the Digestive Tract</p> <ul style="list-style-type: none"> Mechanoreceptors <ul style="list-style-type: none"> • Muscle (stretch, tension, length) • Mucosal Chemoreceptors <ul style="list-style-type: none"> • Acid • Osmotic • Amino acid • Lipid • Glucose Thermoreceptors Pain (?) <p>R B22</p>
<p>B23</p>	<p>Sensory Receptors Transform Changes in Stimulus Energy into Action Potential Codes</p>	 <p>Sensory Receptors Transform Changes in Stimulus Energy into Action Potential Codes</p> <p>The diagram shows a sensory receptor receiving mechanical and chemical stimuli. These stimuli are conducted along the nerve fiber, leading to the generation of a generator potential. Once the generator potential reaches the firing threshold, an action potential is triggered. The firing frequency (action potentials/sec.) increases with stimulus intensity, as shown in the calibration curve graph.</p> <p>R B23</p>

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<p>B24</p>	<p>Sensory Afferents Transmit Signals to Both ENS and CNS</p>	<p>Sensory Afferents Transmit Signals to Both ENS and CNS</p> <p>R B24</p>
<p>B25</p>	<p>Serotonergic 5-HT₃ Receptors Are Expressed on Digestive Tract Afferents</p>	<p>Serotonergic 5-HT₃ Receptors Are Expressed on Digestive Tract Afferents</p> <p>R B25</p>
<p>B26</p>	<p>Distension of the Esophagus Evokes Firing In Vagal Afferent Fibers</p>	<p>Distension of the Esophagus Evokes Firing in Vagal Afferent Fibers</p> <p>Spike discharge in vagal afferent (opossum)</p> <p>R B26</p>

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<p>B27</p>	<p>Low and High Threshold Enteric Mechanosensitive Neurons Project Sensory Information from Large Intestine to Spinal Cord</p>	<p>Low- and High-Threshold Enteric Mechanosensitive Neurons Project Sensory Information From Large Intestine to Spinal Cord</p>  <p>Recording from pelvic nerve afferent fibers during colorectal distension in rat B27</p>
<p>B28</p>	<p>Spinal Gating for Three Classes of Sensory Receptors (Low, High and Silent) Accounts for Normal Regulatory Functions, and Acute and Chronic Pain</p>	<p>Spinal Gating for Three Classes of Sensory Receptors (Low, High, and Silent) Accounts for Normal Regulatory Functions and Acute and Chronic Pain</p>  <p>● Second-order, active neuron ● Second-order, inactive neuron</p> <p>Threshold Low High Silent Normal sensation (No pain) High Intensity (Acute pain) Inflammation (Chronic pain) B28</p>
<p>B29</p>	<p>Enteroendocrine Cells Are the First Step in the Transduction of Chemoreceptive Sensory Information</p>	<p>Enteroendocrine Cells Are the First Step in the Transduction of Chemoreceptive Sensory Information</p>  <p>Lipids Mucosal enterochromaffin cell Cholecystokinin* (CCK) Vagal afferent CCK receptor Vagal afferent Nodose ganglion Dorsal vagal complex ENS B29</p>

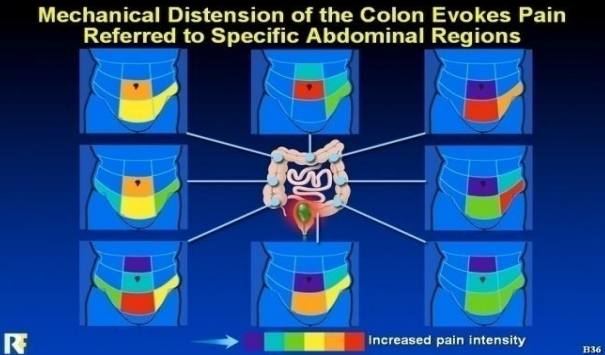
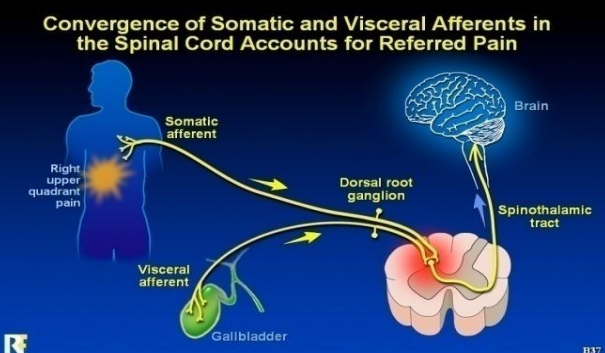
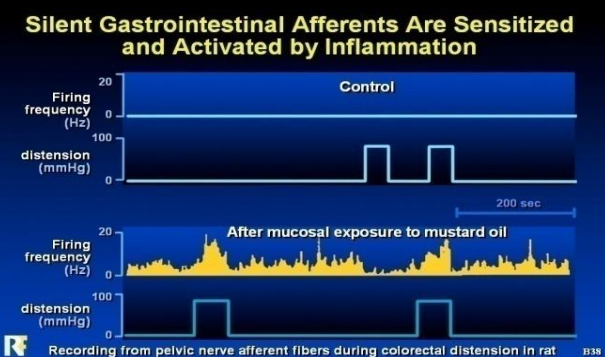
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<p>B30</p>	<p>Chemoreceptors for Acid in the Gastric or Duodenal Mucosa Evoke Firing in Vagal Afferents</p>	<p>Chemoreceptors for Acid in the Gastric or Duodenal Mucosa Evoke Firing in Vagal Afferents</p> <p>The diagram illustrates the firing patterns of vagal afferents. The top section shows 'HCl in stomach' with a high-frequency burst of action potentials (yellow line) followed by a sustained, lower-frequency firing. The bottom section shows 'HCl in duodenum' with a similar but slightly lower-frequency firing pattern. A 1-second scale bar is provided for both sections. The label 'Vagal Afferent Discharge' is centered above the plots.</p>
<p>B31</p>	<p>Sensory Signals Are Processed in Spinal Cord, Brain Stem, and Brain</p>	<p>Sensory Signals Are Processed in Spinal Cord, Brain Stem, and Brain</p> <p>This diagram shows the anatomical pathway of sensory signals. It starts at the 'Abdominal Viscus', travels through the 'Spinal afferent' in the 'Dorsal Root' of the 'Spinal Cord'. From there, it ascends through the 'Dorsal column nociceptive pathway' to the 'Brain Stem', specifically the 'Gracilis and cuneatus nuclei'. Other pathways shown include the 'Lat. spinothalamic tract' and the 'Spinoreticular tract'.</p>
<p>B32</p>	<p>Spinal Pain Circuits</p>	<p>Spinal Pain Circuits</p> <p>The diagram details the neural circuitry of pain. A 'Primary afferent neuron' (yellow) enters the 'Dorsal horn of spinal cord' and releases 'Glutamate substance P' (+) to excite a 'Second-order sensory neuron' (blue). This second-order neuron has two main paths: one that ascends ipsilaterally in the 'Dorsal column' to 'Higher brain centers', and another that synapses with an 'Interneuron' (purple). The interneuron releases 'Enkephalin' (-) to inhibit the second-order neuron and also sends signals to the 'Brain stem'. The brain stem sends 'Descending neuron' (green) signals back to the interneuron, which then releases 'Serotonin Norepinephrine' (+) to further modulate the pathway. The 'Spinothalamic tract' is shown crossing to the 'Contralateral cord'.</p>

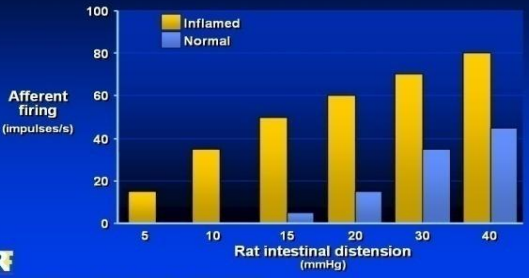
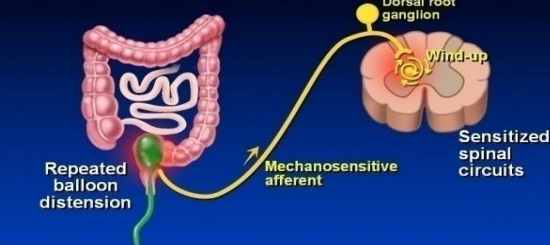
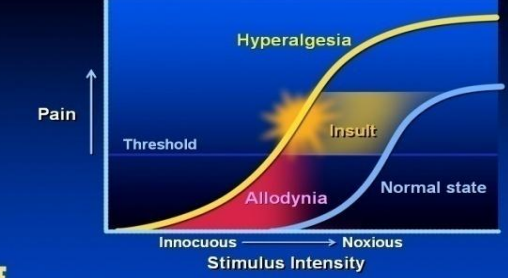
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<p>B33</p>	<p>Visceral Sensory Pathways: Ascending Pathways</p>	<p>Visceral Sensory Pathways</p> <p>Ascending pathways</p> <p>Ipsilateral spinal cord</p> <p>Dorsal column</p> <p>Dorsal columns</p> <p>DRG</p> <p>Spinal afferents</p> <p>Midline</p> <p>Contralateral spinal cord</p> <p>Anterior spinothalamic pathway</p> <p>Brain stem reticular formation</p> <p>Intralaminar thalamic</p> <p>Midbrain tectum</p> <p>Ventral posterior lateral thalamic</p> <p>Somatosensory cortex</p> <p>Posterior parietal cortex</p> <p>Posterior thalamic</p> <p>R B33</p>
<p>B34</p>	<p>Ascending Visceral Pain Pathway</p>	<p>Ascending Visceral Pain Pathway</p> <p>MCC</p> <p>Primary somatosensory cortex</p> <p>pACC</p> <p>Insula</p> <p>Thalamus</p> <p>Reticulothalamic</p> <p>Spinothalamic</p> <p>Spinoreticular</p> <p>Spinomesencephalic</p> <p>Dorsal reticular nucleus</p> <p>Test balloon</p> <p>Rectosigmoid</p> <p>Spinal afferent</p> <p>Spinal cord</p> <p>R B34</p>
<p>B35</p>	<p>Descending Pain Modulation</p>	<p>Descending Pain Modulation</p> <p>ACC</p> <p>Thalamus</p> <p>PAG</p> <p>Locus coeruleus</p> <p>Caudal raphe nucleus</p> <p>Amygdala</p> <p>Rostral ventral medulla</p> <p>Noradrenergic</p> <p>Serotonergic</p> <p>Opioid</p> <p>Test balloon</p> <p>Rectosigmoid</p> <p>Spinal afferent</p> <p>Spinal cord</p> <p>R B35</p>

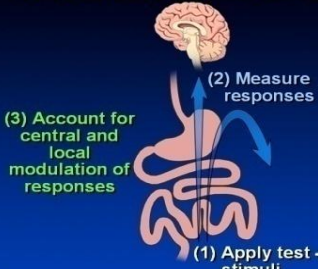
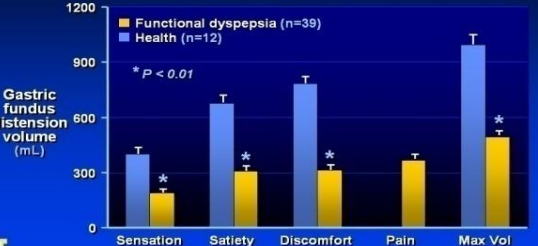
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B36	Mechanical Distention of the Colon Evokes Pain Referred to Specific Abdominal Regions	 <p>Mechanical Distention of the Colon Evokes Pain Referred to Specific Abdominal Regions</p> <p>The diagram illustrates the relationship between colonic distention and referred pain. A central anatomical drawing of the colon is surrounded by nine abdominal diagrams. Each diagram shows a specific region of the abdomen highlighted in a color corresponding to the pain intensity scale. A color bar at the bottom indicates that red represents the highest pain intensity, while blue represents the lowest. A legend 'R' is in the bottom left corner, and the number 'B36' is in the bottom right corner.</p>
B37	Convergence of Somatic and Visceral Afferents in the Spinal Cord Accounts for Referred Pain	 <p>Convergence of Somatic and Visceral Afferents in the Spinal Cord Accounts for Referred Pain</p> <p>This diagram shows the neural pathways for somatic and visceral afferents. A somatic afferent from the right upper quadrant pain area and a visceral afferent from the gallbladder converge in the dorsal root ganglion of the spinal cord. The signals then travel through the spinothalamic tract to the brain. A legend 'R' is in the bottom left corner, and the number 'B37' is in the bottom right corner.</p>
B38	Silent Gastrointestinal Afferents are Sensitized and Activated by Inflammation	 <p>Silent Gastrointestinal Afferents Are Sensitized and Activated by Inflammation</p> <p>The graph displays firing frequency (Hz) and distension (mmHg) over time. The top panel, labeled 'Control', shows a baseline firing frequency of 0 Hz and two square-wave pulses of distension (100 mmHg) that do not elicit any firing. The bottom panel, labeled 'After mucosal exposure to mustard oil', shows a baseline firing frequency of approximately 10 Hz. The same two distension pulses now elicit a significant increase in firing frequency, reaching about 20 Hz. A 200-second scale bar is provided. A legend 'R' is in the bottom left corner, and the number 'B38' is in the bottom right corner.</p>

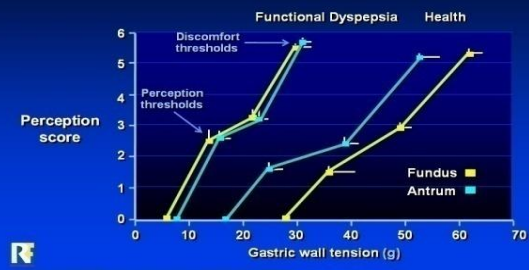
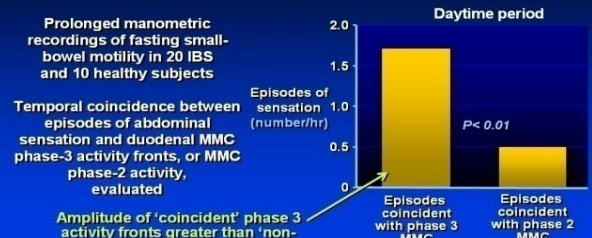
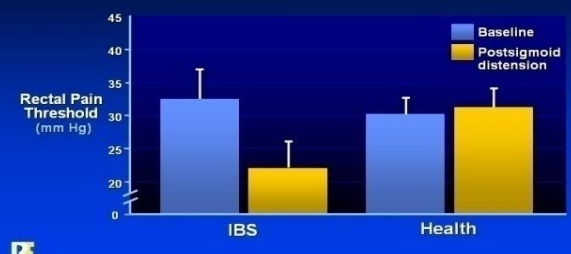
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B39	Gastrointestinal Sensory Afferents are Sensitized by Inflammation	<p>Gastrointestinal Sensory Afferents Are Sensitized by Inflammation</p>  <p>A bar chart with a blue background. The y-axis is labeled 'Afferent firing (impulses/s)' and ranges from 0 to 100 in increments of 20. The x-axis is labeled 'Rat intestinal distension (mmHg)' and has values 5, 10, 15, 20, 30, and 40. There are two data series: 'Inflamed' (yellow bars) and 'Normal' (blue bars). The 'Inflamed' series shows a steady increase in firing rate from approximately 15 impulses/s at 5 mmHg to 80 impulses/s at 40 mmHg. The 'Normal' series shows a much lower firing rate, starting at about 5 impulses/s at 15 mmHg and reaching about 45 impulses/s at 40 mmHg.</p> <table border="1"><thead><tr><th>Rat intestinal distension (mmHg)</th><th>Inflamed (impulses/s)</th><th>Normal (impulses/s)</th></tr></thead><tbody><tr><td>5</td><td>15</td><td>0</td></tr><tr><td>10</td><td>35</td><td>0</td></tr><tr><td>15</td><td>50</td><td>5</td></tr><tr><td>20</td><td>60</td><td>15</td></tr><tr><td>30</td><td>70</td><td>35</td></tr><tr><td>40</td><td>80</td><td>45</td></tr></tbody></table> <p><small>Coutinho SV et al. Prog Brain Res 2000; 29:375</small></p>	Rat intestinal distension (mmHg)	Inflamed (impulses/s)	Normal (impulses/s)	5	15	0	10	35	0	15	50	5	20	60	15	30	70	35	40	80	45
Rat intestinal distension (mmHg)	Inflamed (impulses/s)	Normal (impulses/s)																					
5	15	0																					
10	35	0																					
15	50	5																					
20	60	15																					
30	70	35																					
40	80	45																					
B40	Repetitive Mechanical Stimulation Sensitizes the Spinal Cord	<p>Repetitive Mechanical Stimulation Sensitizes the Spinal Cord</p>  <p>A diagram showing a cross-section of the spinal cord. On the left, a pink balloon is shown distending the intestines, labeled 'Repeated balloon distension'. A yellow line representing a 'Mechanosensitive afferent' leads from the intestines to the 'Dorsal root ganglion'. Inside the ganglion, a yellow spiral is labeled 'Wind-up'. The signal then enters the spinal cord, where it is labeled 'Sensitized spinal circuits'.</p>																					
B41	The Phenomena of Hyperalgesia and Allodynia	<p>The Phenomena of Hyperalgesia and Allodynia</p>  <p>A graph with a blue background. The y-axis is labeled 'Pain' and has an upward arrow. The x-axis is labeled 'Stimulus Intensity' and ranges from 'Innocuous' on the left to 'Noxious' on the right. A horizontal line represents the 'Threshold'. Two curves are shown: a blue curve for 'Normal state' and a yellow curve for 'Hyperalgesia'. The yellow curve is shifted upwards and to the left, crossing the threshold at a lower stimulus intensity. A red area between the curves is labeled 'Allodynia'. A yellow starburst labeled 'Insult' is shown above the threshold line.</p>																					

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<p>B42</p>	<p>Schema for Evaluation of Enteric Sensation and Reflexes in the Functional GI Disorders</p>	<p>Schema for Evaluation of Enteric Sensation and Reflexes in the Functional GI Disorders</p>  <p>(1) Apply test stimuli</p> <ul style="list-style-type: none"> Physiological e.g., oral or intraluminal nutrients Supraphysiological e.g., gut distension <p>(2) Measure responses</p> <ul style="list-style-type: none"> Conscious perception Afferent signals in brain, spinal cord Autonomic responses Reflex gut motor activity <p>(3) Account for central and local modulation of responses</p> <p><small>B42</small></p>																		
<p>B43</p>	<p>Visceral Hypersensitivity to Gut Distension in the Functional GI Disorders</p>	<p>Visceral Hypersensitivity to Gut Distension in the Functional GI Disorders</p> <ul style="list-style-type: none"> • Frequent and reproducible finding • Organ-specific or pan-intestinal • Enhanced by nutrients (e.g., lipid) • Associated with abnormal viscerosomatic referral and/or somatic hypersensitivity in some patients • Influenced by cognitive and psychological factors (e.g., emotional arousal, vigilance, affect) <p><small>B43</small></p>																		
<p>B44</p>	<p>Patients with Functional Dyspepsia Can Exhibit a Reduced Tolerance to Fundic Distension</p>	<p>Patients With Functional Dyspepsia Can Exhibit a Reduced Tolerance to Fundic Distension</p>  <table border="1"> <caption>Gastric fundus distension volume (mL)</caption> <thead> <tr> <th>Category</th> <th>Functional dyspepsia (n=39)</th> <th>Health (n=12)</th> </tr> </thead> <tbody> <tr> <td>Sensation</td> <td>~150*</td> <td>~400</td> </tr> <tr> <td>Satiety</td> <td>~300*</td> <td>~650</td> </tr> <tr> <td>Discomfort</td> <td>~300*</td> <td>~750</td> </tr> <tr> <td>Pain</td> <td>~350</td> <td>~350</td> </tr> <tr> <td>Max Vol</td> <td>~500*</td> <td>~950</td> </tr> </tbody> </table> <p>* P < 0.01</p> <p><small>Bouin M et al. Eur J Gastroenterol 2006; 18:63</small></p> <p><small>B44</small></p>	Category	Functional dyspepsia (n=39)	Health (n=12)	Sensation	~150*	~400	Satiety	~300*	~650	Discomfort	~300*	~750	Pain	~350	~350	Max Vol	~500*	~950
Category	Functional dyspepsia (n=39)	Health (n=12)																		
Sensation	~150*	~400																		
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<p>B45</p>	<p>Functional Dyspepsia Patients Show Increased Antral, as Well as Fundic, Sensitivity to Distention</p>	<p>Functional Dyspepsia Patients Show Increased Antral, As Well As Fundic, Sensitivity to Distention</p>  <p>The graph plots Perception score (0-6) against Gastric wall tension (g) (0-70). Two lines represent 'Fundus' (red) and 'Antrum' (green). Two sets of curves are shown: 'Discomfort thresholds' (higher) and 'Perception thresholds' (lower). In Functional Dyspepsia, both thresholds are significantly lower than in Health. The legend indicates Fundus (red square) and Antrum (green square).</p> <p><i>Caldarella MP Gastroenterology 2003; 124:1220</i></p> <p>B45</p>
<p>B46</p>	<p>Enhanced Perception of Physiological Intestinal Motility, Not Only Balloon Distension, Occurs in IBS</p>	<p>Enhanced Perception of Physiological Intestinal Motility, Not Only Balloon Distension, Occurs in IBS</p> <p>Prolonged manometric recordings of fasting small-bowel motility in 20 IBS and 10 healthy subjects</p> <p>Temporal coincidence between episodes of abdominal sensation and duodenal MMC phase-3 activity fronts, or MMC phase-2 activity, evaluated</p> <p>Amplitude of 'coincident' phase 3 activity fronts greater than 'non-coincident' fronts</p>  <p>The bar chart shows 'Episodes of sensation (number/hr)' for 'Daytime period'. The y-axis ranges from 0 to 2.0. Two bars are shown: 'Episodes coincident with phase 3 MMC' (red bar, ~1.7) and 'Episodes coincident with phase 2 MMC' (blue bar, ~0.5). A p-value of <math>P < 0.01</math> is indicated between the bars.</p> <p><i>Kellow J et al. Gastroenterology 1991; 101:1621</i></p> <p>B46</p>
<p>B47</p>	<p>Rectal Hypersensitivity in IBS is Provoked by Repetitive Sigmoid Colon Distension</p>	<p>Rectal Hypersensitivity in IBS is Provoked by Repetitive Sigmoid Colon Distension</p>  <p>The bar chart shows 'Rectal Pain Threshold (mm Hg)' for 'IBS' and 'Health' groups. The y-axis ranges from 0 to 45. For each group, two bars are shown: 'Baseline' (red) and 'Postsigmoid distension' (blue). In the IBS group, the threshold drops from ~33 mm Hg at baseline to ~23 mm Hg post-distension. In the Health group, the threshold remains relatively stable, dropping slightly from ~30 mm Hg at baseline to ~31 mm Hg post-distension.</p> <p><i>Munakata J Gastroenterology 1997; 112:55</i></p> <p>B47</p>

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<p>B48</p>	<p>Functional Dyspepsia Patients, As Well As IBS, Exhibit Rectal Hypersensitivity</p>	<p>Functional Dyspepsia Patients, As Well As IBS, Exhibit Rectal Hypersensitivity</p> <p>Perception: Health (246), IBS, Functional dyspepsia (198). P-values: Health vs IBS ($P < 0.0001$), Health vs Functional dyspepsia ($P < 0.001$).</p> <p>Urgency: Health, IBS, Functional dyspepsia. P-values: Health vs IBS ($P < 0.0001$), Health vs Functional dyspepsia ($P < 0.0001$).</p> <p>Trimble et al. Dig Dis Sci 1995; 40:1607</p>												
<p>B49</p>	<p>IBS Patients, As Well As Functional Dyspepsia, Exhibit Esophageal Hypersensitivity</p>	<p>IBS Patients, As Well As Functional Dyspepsia, Exhibit Esophageal Hypersensitivity</p> <p>Perception: Health, IBS, Functional dyspepsia. P-values: Health vs IBS ($P < 0.05$), Health vs Functional dyspepsia ($P < 0.02$).</p> <p>Discomfort: Health, IBS, Functional dyspepsia. P-values: Health vs IBS ($P < 0.02$), Health vs Functional dyspepsia ($P < 0.001$).</p> <p>Trimble et al. Dig Dis Sci 1995; 40:1607</p>												
<p>B50</p>	<p>Type of Functional GI Disorder Determines Pattern of Gastric and Rectal Hypersensitivity</p>	<p>Type of Functional GI Disorder Determines Pattern of Gastric and Rectal Hypersensitivity</p> <table border="1"> <thead> <tr> <th>Disorder</th> <th>Stomach (%)</th> <th>Rectum (%)</th> </tr> </thead> <tbody> <tr> <td>Functional dyspepsia</td> <td>~90</td> <td>~20</td> </tr> <tr> <td>IBS</td> <td>~15</td> <td>~85</td> </tr> <tr> <td>FD + IBS</td> <td>~80</td> <td>~90</td> </tr> </tbody> </table> <p>Boulin M et al. Neurogastroenterol Motil 2004; 16:311</p>	Disorder	Stomach (%)	Rectum (%)	Functional dyspepsia	~90	~20	IBS	~15	~85	FD + IBS	~80	~90
Disorder	Stomach (%)	Rectum (%)												
Functional dyspepsia	~90	~20												
IBS	~15	~85												
FD + IBS	~80	~90												

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<p>B51</p>	<p>Colonic and Rectal Sensitivity, Both Pain and Non-Pain, to Phasic Distension are Correlated in IBS</p>	<p>Colonic and Rectal Sensitivity, Both Pain and Non-Pain, to Phasic Distension Are Correlated in IBS</p> <p>20 IBS patients Phasic barostat distension both colon and rectum Visual analogue scale for pain and non-pain</p> <p>Rectum can serve as a legitimate 'window' to evaluate colonic hypersensitivity in IBS</p> <p>Phasic distension (16 mmHg)</p> <p>Colon (VAS)</p> <p>Rectum (VAS)</p> <p>Pain $r=0.60, P=0.006$ Non-pain $r=0.59, P=0.006$</p> <p>Ng C et al. <i>Neurogastroenterol Motil</i> 2006; 18:206</p> <p>B51</p>
<p>B52</p>	<p>Colonic Hypersensitivity to Barostat Distension in IBS is Increased After Duodenal Lipid Infusion</p>	<p>Colonic Hypersensitivity to Barostat Distension in IBS Is Increased After Duodenal Lipid Infusion</p> <p>IBS patients (n=61) Healthy subjects (n=20)</p> <p>% subjects reporting pain</p> <p>Balloon pressure (mmHg)</p> <p>After lipids Before lipids</p> <p>Colonic hypersensitivity in IBS is not influenced by predominant bowel pattern, psychological factors, or gender</p> <p>Simrén M et al. <i>Clin Gastroenterol Hepatol</i>. 2007; 5:201</p> <p>B52</p>
<p>B53</p>	<p>Colonic Distension Postprandially Provokes an Altered Autonomic Response in IBS</p>	<p>Colonic Distension Postprandially Provokes an Altered Autonomic Response in IBS</p> <ul style="list-style-type: none"> • 8 IBS and 8 healthy subjects • Descending colon barostat phasic distension (2 min) • Heart rate variability recorded: LF/HF ratio (sympathovagal balance) <p>Change in LF/HF ratio during distension</p> <p>Fasting Postprandial</p> <p>IBS Health</p> <p>Postprandial LF/HF ratio change in IBS is independent of colonic sensitivity or distending volume</p> <p>Ng C et al. <i>Scand J Gastroenterol</i> 2007; 42:441</p> <p>B53</p>

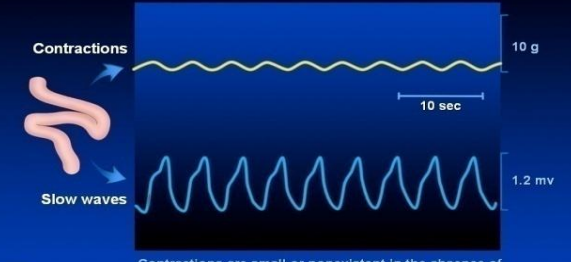
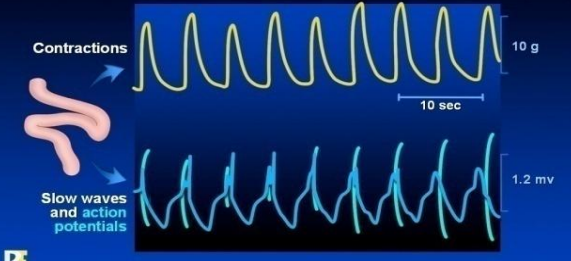
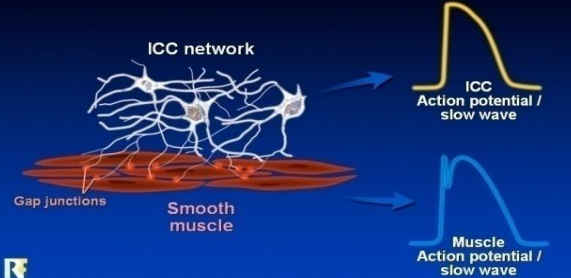
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<p>B54</p>	<p>Rectal Hypersensitivity in IBS is Associated With Greater Symptom Severity</p>	<p>Rectal Hypersensitivity in IBS is Associated With Greater Symptom Severity</p> <p>Pain and bloating independently associated with rectal hypersensitivity ($r^2=0.22$)</p> <p>% patients with \geq moderate symptom severity</p> <p>Legend: Rectal hypersensitivity (n=67) [Yellow], Normal sensitivity (n=42) [Blue]</p> <p>Significance: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$</p> <p>Posserud J et al. <i>Gastroenterology</i> 2007; 133:1113</p>
<p>B55</p>	<p>Hypersensitivity to Rectal Distension in IBS: Shorter Latencies of Cerebral Evoked Potentials</p>	<p>Hypersensitivity to Rectal Distension in IBS: Shorter Latencies of Cerebral Evoked Potentials</p> <p>Cerebral EPs recorded in response to rhythmic balloon distension of rectum</p> <p>EP latency (msec)</p> <p>$P = 0.0001$</p> <p>Health (n=22) [Blue line], IBS (n=22) [Yellow line]</p> <p>Similar findings postprandially</p> <p>Chan Y-K et al. <i>Am J Gastroenterol</i> 2001; 96:2413</p>
<p>B56</p>	<p>Rectal Barostat Sensory Testing in IBS: Sensitivity and Specificity</p>	<p>Rectal Barostat Sensory Testing in IBS: Sensitivity and Specificity</p> <p>%</p> <p>Rectal pain threshold (mmHg)</p> <p>Legend: Specificity [Yellow line], Sensitivity [Green line], Negative predictive value [Red line]</p> <p>Boulin M et al. <i>Gastroenterology</i> 2002; 122:1771</p>

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<p>B57</p>	<p>Colonic Hypersensitivity in IBS: Influenced Strongly by a Psychological Tendency to Report Pain Rather than Increased Neurosensory Sensitivity</p>	<p>Colonic Hypersensitivity in IBS: Influenced Strongly by a Psychological Tendency to Report Pain Rather Than Increased Neurosensory Sensitivity</p> <p>Colonic pain threshold (mmHg): IBS (~28), Health (~40), $P < 0.0001$</p> <p>Pain-reporting tendency (report criterion): IBS (~4), Health (~5), $P < 0.03$</p> <p>Neurosensory sensitivity (discrimination index [pA]): IBS (~0.5), Health (~0.5), NS</p> <p><small>Dorn S et al. Gut 2007; 56:1202</small></p>
<p>B58</p>	<p>Section Title: Motility and Dysmotility: Fundamental Concepts</p>	
<p>B59</p>	<p>Gastrointestinal Smooth Muscles Have Properties of a Functional Electrical Syncytium</p>	<p>Gastrointestinal Smooth Muscles Have Properties of a Functional Electrical Syncytium</p> <p>Electrical activity</p> <p>Gap junction</p> <p>Gap junction channels</p> <p>Gap junctions pass electrical current from muscle fiber to muscle fiber</p> <p><small>B59</small></p>
<p>B60</p>	<p>Electrical Activity Occurs at Different Frequencies in Stomach, Small Intestine, and Colon</p>	<p>Electrical Activity Occurs at Different Frequencies in Stomach, Small Intestine, and Colon</p> <p>Stomach: -30 mv</p> <p>Small intestine: -22 mv</p> <p>Colon: -41 mv, -81 mv</p> <p>30 sec</p> <p>Frequency of contractions follows the frequency of electrical activity</p> <p><small>B60</small></p>

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B61	Electrical Slow Waves Without Action Potentials Are Often Present in the Small Intestine	<p>Electrical Slow Waves Without Action Potentials Are Often Present in the Small Intestine</p>  <p>The diagram shows a small intestine on the left. Two traces are shown: 'Contractions' (top) and 'Slow waves' (bottom). The contraction trace shows small, irregular waves with a 10 g scale bar. The slow wave trace shows regular, rhythmic waves with a 1.2 mV scale bar. A 10 sec scale bar is also present. A caption at the bottom states: 'Contractions are small or nonexistent in the absence of action potentials when recorded extracellularly'. A small 'R' logo is in the bottom left, and 'B61' is in the bottom right.</p>
B62	Contractions Are Seen When Action Potentials Appear on Slow Waves	<p>Contractions Are Seen When Action Potentials Appear on Slow Waves</p>  <p>The diagram shows a small intestine on the left. Two traces are shown: 'Contractions' (top) and 'Slow waves and action potentials' (bottom). The contraction trace shows large, regular waves with a 10 g scale bar. The slow wave trace shows regular waves with sharp upward spikes (action potentials) and a 1.2 mV scale bar. A 10 sec scale bar is also present. A small 'R' logo is in the bottom left, and 'B62' is in the bottom right.</p>
B63	Networks of Interstitial Cells of Cajal are Pacemakers for Electrical Activity in the Gastrointestinal Musculature	<p>Networks of Interstitial Cells of Cajal Are Pacemakers for Electrical Activity in the Gastrointestinal Musculature</p>  <p>The diagram shows a network of Interstitial Cells of Cajal (ICC) connected by gap junctions, situated above smooth muscle. An arrow points from the ICC network to a graph of an 'ICC Action potential / slow wave', which shows a slow depolarization followed by a sharp spike. Another arrow points from the smooth muscle to a graph of a 'Muscle Action potential / slow wave', which shows a similar slow depolarization followed by a sharp spike. A small 'R' logo is in the bottom left, and 'B63' is in the bottom right.</p>

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<p>B64</p>	<p>Activity of Inhibitory Motor Neurons to the Intestinal Circular Muscle Tonicly Inhibits Contractions</p>	<p>Activity of Inhibitory Motor Neurons to the Intestinal Circular Muscle Tonicly Inhibits Contractions</p> <p>Contractile strength</p> <p>Inhibitory neurons in "active state"</p> <p>Some neurons "inactive"</p> <p>More neurons "inactive"</p> <p>Most neurons "inactive"</p> <p>Slow waves and action potentials</p> <p>Progressive neural blockade - tetrodotoxin</p> <p>10 sec</p> <p>R</p> <p>B64</p>
<p>B65</p>	<p>Inhibitory Innervation of Sphincters is Continuously Inactive and Transiently Activated for Timed Opening</p>	<p>Inhibitory Innervation of Sphincters is Continuously Inactive and Transiently Activated for Timed Opening</p> <p>Lower esophageal sphincter contracted</p> <p>Pylorus sphincter contracted</p> <p>Internal anal sphincter contracted</p> <p>Inhibitory musclemotor neurons</p> <p>Inactive</p> <p>Active</p> <p>Lower esophageal sphincter relaxed</p> <p>Pylorus sphincter relaxed</p> <p>Internal anal sphincter relaxed</p> <p>R</p> <p>B65</p>
<p>B66</p>	<p>Inhibitory Motor Innervation of the Intestinal Circular Muscle Is Continuously Active and Is Transiently Inactivated to Permit Muscle Contraction</p>	<p>Inhibitory Motor Innervation of the Intestinal Circular Muscle Is Continuously Active and Is Transiently Inactivated to Permit Muscle Contraction</p> <p>Contractile state of intestine</p> <p>Absence of contraction</p> <p>Contraction</p> <p>Absence of contraction</p> <p>Activity status of inhibitory musclemotor neurons</p> <p>Active</p> <p>Inactive</p> <p>Active</p> <p>R</p> <p>B66</p>

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<p>B67</p>	<p>Enteric Nervous System Contains a Library of Programs for Specific Patterns of Intestinal Motor Behavior</p>	<p>Enteric Nervous System Contains a Library of Programs for Specific Patterns of Intestinal Motor Behavior</p> <p>Small intestine Postprandial program (Mixing pattern)</p> <p>Small intestine Interdigestive program (MMC pattern)</p> <p>Small and large intestine Physiologic ileus (Contraction absent)</p> <p>Large intestine Haustral program (Haustra)</p> <p>Small and large intestine Defense program Aboral power propulsion program</p> <p>Small intestine Defense program Oral power propulsion (Emetic program)</p> <p>R B67</p>										
<p>B68</p>	<p>Gastrointestinal Motility and ENS-CNS Control</p>	<p>Gastrointestinal Motility and ENS-CNS Control</p> <p>Interdigestive Primary peristalsis CNS Postprandial</p> <p>Receptive & adaptive gastric reservoir relaxation; regular antral contractions</p> <p>Periodic motor activity (migrating motor complex) ENS modulated by CNS</p> <p>Vagal mediation Irregular nonperiodic motor activity ENS modulated by vagal receptors</p> <p>Sporadic motor activity, reduced in sleep; occasional HAPCs ENS modulated by CNS</p> <p>Increased HAPCs, phasic contractions, and tone ENS modulated by CNS</p> <p>Defecation ENS + CNS</p> <p>R B68</p>										
<p>B69</p>	<p>Measurement of Digestive Tract Motility: Transit I</p>	<p>Measurement of Digestive Tract Motility: Transit I</p> <table border="1"> <thead> <tr> <th>Recording technique</th> <th>Main applications</th> </tr> </thead> <tbody> <tr> <td>Radiopaque markers x-ray</td> <td>Colonic transit</td> </tr> <tr> <td>Hydrogen breath tests</td> <td>Orocecal transit</td> </tr> <tr> <td>Scintigraphy</td> <td>Esophageal transit Gastric emptying Small-bowel and colonic transit Bile flow Defecation dynamics</td> </tr> <tr> <td>Labeled C-substrate breath tests</td> <td>Gastric emptying Orocecal transit</td> </tr> </tbody> </table> <p>R B69</p>	Recording technique	Main applications	Radiopaque markers x-ray	Colonic transit	Hydrogen breath tests	Orocecal transit	Scintigraphy	Esophageal transit Gastric emptying Small-bowel and colonic transit Bile flow Defecation dynamics	Labeled C-substrate breath tests	Gastric emptying Orocecal transit
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<p>B70</p>	<p>Measurement of Digestive Tract Motility: Transit II</p>	<p style="text-align: center;">Measurement of Digestive Tract Motility: Transit II</p> <table border="0"> <thead> <tr> <th style="text-align: left;">Recording technique</th> <th style="text-align: left;">Main applications</th> </tr> </thead> <tbody> <tr> <td>Intraluminal impedance monitoring</td> <td>Esophageal transit</td> </tr> <tr> <td>Pharmacologic markers Acetaminophen Sulfasalazine</td> <td>Gastric emptying of liquids Orocecal transit time</td> </tr> <tr> <td>Magnetic resonance imaging</td> <td>Gastric emptying</td> </tr> </tbody> </table> <p>R B70</p>	Recording technique	Main applications	Intraluminal impedance monitoring	Esophageal transit	Pharmacologic markers Acetaminophen Sulfasalazine	Gastric emptying of liquids Orocecal transit time	Magnetic resonance imaging	Gastric emptying
Recording technique	Main applications									
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Pharmacologic markers Acetaminophen Sulfasalazine	Gastric emptying of liquids Orocecal transit time									
Magnetic resonance imaging	Gastric emptying									
<p>B71</p>	<p>Measurement of Digestive Tract Motility: Intraluminal Pressure</p>	<p style="text-align: center;">Measurement of Digestive Tract Motility: Intraluminal Pressure</p> <table border="0"> <thead> <tr> <th style="text-align: left;">Recording technique</th> <th style="text-align: left;">Main applications</th> </tr> </thead> <tbody> <tr> <td>Water- perfused manometry: Stationary (or ambulant)</td> <td>Phasic contractions at all levels of digestive tract</td> </tr> <tr> <td>Solid-state microtransducer manometry: Stationary or ambulant</td> <td>Phasic contractions at all levels of digestive tract</td> </tr> </tbody> </table> <p>R B71</p>	Recording technique	Main applications	Water- perfused manometry: Stationary (or ambulant)	Phasic contractions at all levels of digestive tract	Solid-state microtransducer manometry: Stationary or ambulant	Phasic contractions at all levels of digestive tract		
Recording technique	Main applications									
Water- perfused manometry: Stationary (or ambulant)	Phasic contractions at all levels of digestive tract									
Solid-state microtransducer manometry: Stationary or ambulant	Phasic contractions at all levels of digestive tract									
<p>B72</p>	<p>Measurement of Digestive Tract Motility: Tone, Compliance and Reflexes</p>	<p style="text-align: center;">Measurement of Digestive Tract Motility: Tone, Compliance, and Reflexes</p> <table border="0"> <thead> <tr> <th style="text-align: left;">Recording technique</th> <th style="text-align: left;">Main applications</th> </tr> </thead> <tbody> <tr> <td>Electronic barostat: Single barostat</td> <td>Tonic contractions Gut compliance</td> </tr> <tr> <td>Dual barostat</td> <td>Intestino-intestinal tonic reflexes</td> </tr> </tbody> </table> <p>R B72</p>	Recording technique	Main applications	Electronic barostat: Single barostat	Tonic contractions Gut compliance	Dual barostat	Intestino-intestinal tonic reflexes		
Recording technique	Main applications									
Electronic barostat: Single barostat	Tonic contractions Gut compliance									
Dual barostat	Intestino-intestinal tonic reflexes									

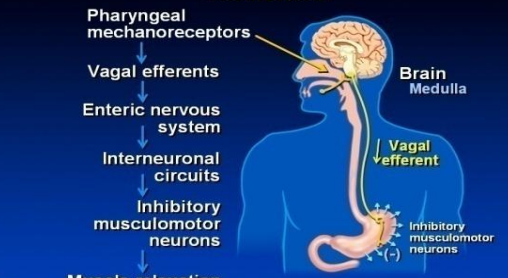
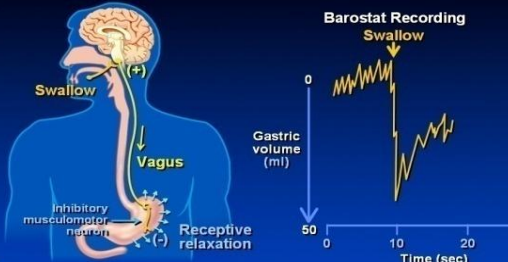
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<p>B73</p>	<p>Measurement of Digestive Tract Motility: Myoelectric Activity</p>	<p style="text-align: center;">Measurement of Digestive Tract Motility: Myoelectric Activity</p> <table border="1"> <thead> <tr> <th>Recording technique</th> <th>Main applications</th> </tr> </thead> <tbody> <tr> <td>Electrogastrography</td> <td>Gastric surface electrical activity</td> </tr> <tr> <td>Intraluminal electromyography</td> <td>Intestinal slow wave, spike bursts</td> </tr> <tr> <td>Needle electromyography</td> <td>Anal sphincter & pelvic floor muscle activity</td> </tr> </tbody> </table> <p>R B73</p>	Recording technique	Main applications	Electrogastrography	Gastric surface electrical activity	Intraluminal electromyography	Intestinal slow wave, spike bursts	Needle electromyography	Anal sphincter & pelvic floor muscle activity		
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Electrogastrography	Gastric surface electrical activity											
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<p>B74</p>	<p>Measurement of Digestive Tract Motility: Wall Motion</p>	<p style="text-align: center;">Measurement of Digestive Tract Motility: Wall Motion</p> <table border="1"> <thead> <tr> <th>Recording technique</th> <th>Main applications</th> </tr> </thead> <tbody> <tr> <td>Ultrasonography</td> <td>Antropyloric contractions Gastric areas and volume Gallbladder volume</td> </tr> <tr> <td>Scintigraphy</td> <td>Antral contractions</td> </tr> <tr> <td>Magnetic resonance imaging</td> <td>Antral contractions</td> </tr> <tr> <td>SPECT</td> <td>Gastric reservoir relaxation</td> </tr> </tbody> </table> <p>R B74</p>	Recording technique	Main applications	Ultrasonography	Antropyloric contractions Gastric areas and volume Gallbladder volume	Scintigraphy	Antral contractions	Magnetic resonance imaging	Antral contractions	SPECT	Gastric reservoir relaxation
Recording technique	Main applications											
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Scintigraphy	Antral contractions											
Magnetic resonance imaging	Antral contractions											
SPECT	Gastric reservoir relaxation											
<p>B75</p>	<p>Gastrointestinal Dysmotility in the Functional Gastrointestinal Disorders (FGIDs)</p>	<p>Part I</p> <p style="text-align: center;">Gastrointestinal Dysmotility in the Functional Gastrointestinal Disorders (FGIDs)</p> <ul style="list-style-type: none"> • Definitive motor abnormalities in the FGIDs are difficult to establish with current technologies • Alterations in motility are documented throughout the gut and in many of the FGIDs, but inconsistencies between studies • Dysmotility in the FGIDs is most prominent in response to enteric and central stimuli (e.g., food, bile salts, hormones, psychologic stress) <p>R B75</p>										

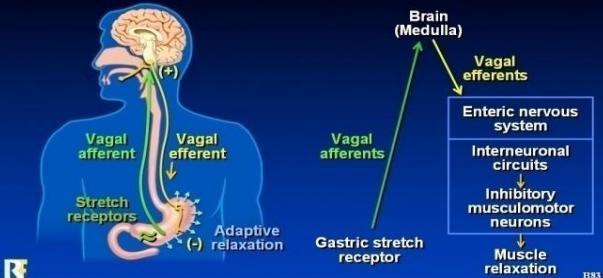

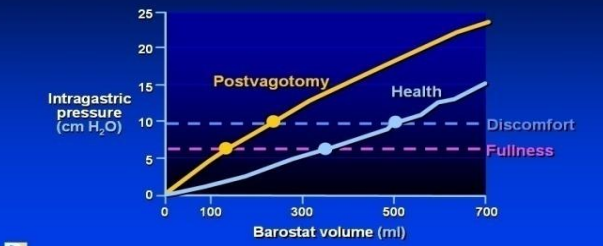
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B76	Gastrointestinal Dysmotility in the Functional Gastrointestinal Disorders (FGIDs)	<p>Part II</p> <h3>Gastrointestinal Dysmotility in the Functional Gastrointestinal Disorders (FGIDs)</h3> <ul style="list-style-type: none">• Correlation is weak between dysmotility and symptoms in most instances• Gastrointestinal transit remains the most useful clinical measure of dysmotility in the FGIDs• Noninvasive and ambulatory measurement techniques are required for further progress• Relationship between dysmotility and visceral hypersensitivity in the FGIDs requires further study <p>R B76</p>
B77	Section Title: Regional Motility - Stomach	
B78	The Stomach Is Divided Into Multiple Anatomic and Only Two Functional Motor Regions	<h3>The Stomach Is Divided Into Multiple Anatomic and Only Two Functional Motor Regions</h3> <p>Anatomic regions: Fundus, Body (corpus), Antrum, Pylorus</p> <p>Functional motor regions: Gastric reservoir (Tonic contractions), Antral pump (Phasic contractions)</p> <p>Functional motor and anatomic regions do not correspond</p> <p>R B78</p>
B79	Control of Muscular Tone Determines Volume in the Gastric Reservoir	<h3>Control of Muscular Tone Determines Volume in the Gastric Reservoir</h3> <p>R Neural mechanisms determine intramural contractile tone in the reservoir B79</p>

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<p>B80</p>	<p>Relaxation in the Gastric Reservoir</p>	<p>Relaxation in the Gastric Reservoir</p> <table border="1"> <thead> <tr> <th>Origin of stimulus</th> <th>Stimulus</th> <th>Relaxation type</th> </tr> </thead> <tbody> <tr> <td> <ul style="list-style-type: none"> • Pharynx • Stomach • Small intestine </td> <td> <ul style="list-style-type: none"> • Swallowing • Gastric distension • Nutrients </td> <td> <ul style="list-style-type: none"> • Receptive • Adaptive • Feedback </td> </tr> </tbody> </table> <p>All three types of relaxation are at least partly mediated by vagus nerves</p> <p>R B80</p>	Origin of stimulus	Stimulus	Relaxation type	<ul style="list-style-type: none"> • Pharynx • Stomach • Small intestine 	<ul style="list-style-type: none"> • Swallowing • Gastric distension • Nutrients 	<ul style="list-style-type: none"> • Receptive • Adaptive • Feedback
Origin of stimulus	Stimulus	Relaxation type						
<ul style="list-style-type: none"> • Pharynx • Stomach • Small intestine 	<ul style="list-style-type: none"> • Swallowing • Gastric distension • Nutrients 	<ul style="list-style-type: none"> • Receptive • Adaptive • Feedback 						
<p>B81</p>	<p>Swallowing Evokes Gastric Receptive Relaxation</p>	<p>Swallowing Evokes Gastric Receptive Relaxation</p>  <p>Pharyngeal mechanoreceptors Vagal efferents Enteric nervous system Interneuronal circuits Inhibitory musculomotor neurons Muscle relaxation</p> <p>Brain Medulla Vagal efferent Inhibitory musculomotor neurons</p> <p>R B81</p>						
<p>B82</p>	<p>Swallowing Evokes Gastric Receptive Relaxation and Increased Gastric Volume</p>	<p>Swallowing Evokes Gastric Receptive Relaxation and Increased Gastric Volume</p>  <p>Swallow Vagus Inhibitory musculomotor neuron Receptive relaxation</p> <p>Barostat Recording Swallow</p> <p>Gastric volume (ml) Time (sec)</p> <p>R B82</p>						

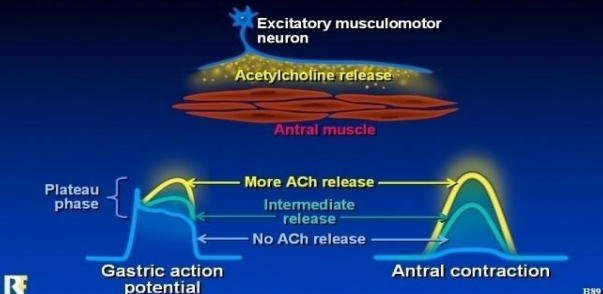
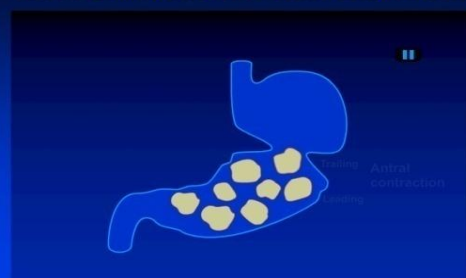
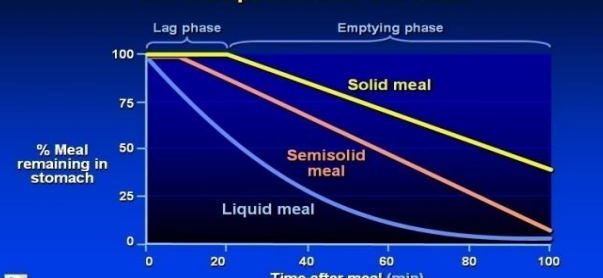
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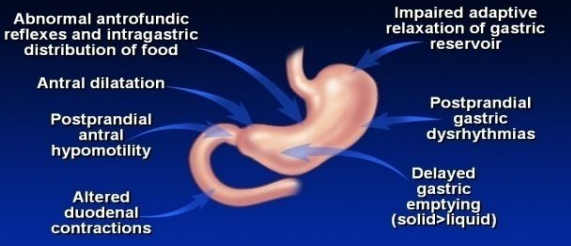
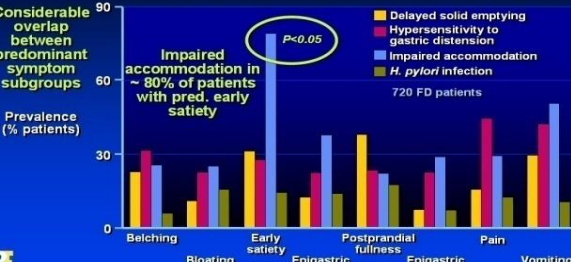
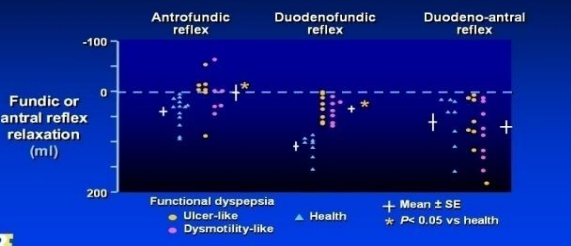
<p>B83</p>	<p>Adaptive Relaxation in the Gastric Reservoir Is a Vago-Vagal Reflex</p>	<p>Adaptive Relaxation in the Gastric Reservoir Is a Vago-Vagal Reflex</p>  <p>B83</p>
<p>B84</p>	<p>Normal Meal-Induced Gastric Accommodation</p>	<p>Normal Meal-Induced Gastric Accommodation</p> <p>14 healthy subjects ingested mixed 200-ml, 300-kcal, liquid meal</p> <p>Proximal gastric barostat balloon</p> <p>Significant gastric reservoir adaptive relaxation during 40-min postmeal recording</p>  <p>B84</p> <p><small>Lee KJ et al. Gut 2004; 53:938</small></p>
<p>B85</p>	<p>Adaptive Relaxation in the Gastric Reservoir Is Absent After Vagotomy</p>	<p>Adaptive Relaxation in the Gastric Reservoir Is Absent After Vagotomy</p>  <p>B85</p>

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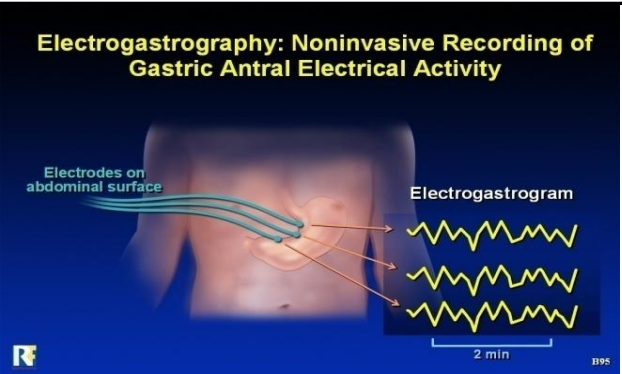
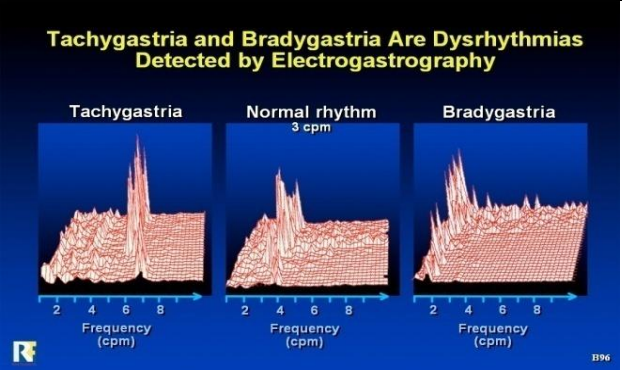
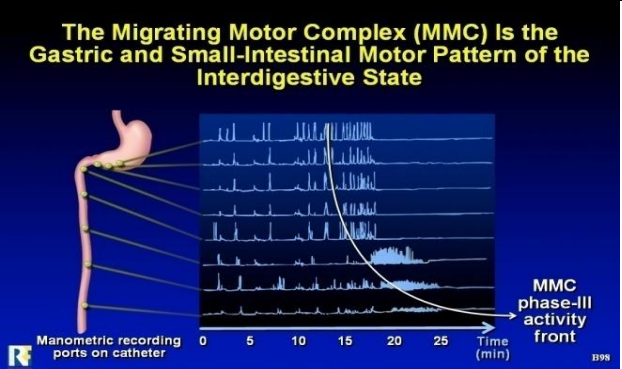
<p>B86</p>	<p>Cholecystokinin (CCK) Is a Chemical Signal from the Duodenum for Feedback Regulation of the Gastric Reservoir</p>	<p>Cholecystokinin (CCK) Is a Chemical Signal from the Duodenum for Feedback Regulation of the Gastric Reservoir</p> <p>Solutions infused into the duodenum at a rate of 1 ml/min</p> <table border="1"> <caption>Estimated data from the graph in slide B86</caption> <thead> <tr> <th>Barostat volume (ml)</th> <th>NaCl (0.9%) (cm H₂O)</th> <th>Lipid (2 kcal/ml) (cm H₂O)</th> <th>Lipid (2 kcal/ml) with antagonist (cm H₂O)</th> </tr> </thead> <tbody> <tr> <td>0</td> <td>0</td> <td>0</td> <td>0</td> </tr> <tr> <td>100</td> <td>~4</td> <td>~2</td> <td>~1</td> </tr> <tr> <td>200</td> <td>~7</td> <td>~4</td> <td>~2</td> </tr> <tr> <td>300</td> <td>~10</td> <td>~6</td> <td>~3</td> </tr> <tr> <td>400</td> <td>~13</td> <td>~8</td> <td>~4</td> </tr> </tbody> </table> <p>R B86</p>	Barostat volume (ml)	NaCl (0.9%) (cm H ₂ O)	Lipid (2 kcal/ml) (cm H ₂ O)	Lipid (2 kcal/ml) with antagonist (cm H ₂ O)	0	0	0	0	100	~4	~2	~1	200	~7	~4	~2	300	~10	~6	~3	400	~13	~8	~4
Barostat volume (ml)	NaCl (0.9%) (cm H ₂ O)	Lipid (2 kcal/ml) (cm H ₂ O)	Lipid (2 kcal/ml) with antagonist (cm H ₂ O)																							
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400	~13	~8	~4																							
<p>B87</p>	<p>Motility of the Antral Pump Is Initiated by a Dominant Pacemaker in the Mid-Corpus</p>	<p>Motility of the Antral Pump Is Initiated by a Dominant Pacemaker in the Mid-Corpus</p> <p>Pacemaker potentials determine contractile parameters</p> <p>Contractile parameters</p> <ul style="list-style-type: none"> •Maximal frequency •Propagation velocity •Propagation direction <p>The antral pump is formed by the mid and distal corpus, antrum, and pylorus</p> <p>R B87</p>																								
<p>B88</p>	<p>Leading and Trailing Antral Contractions Are Initiated by an Action Potential</p>	<p>Leading and Trailing Antral Contractions Are Initiated by an Action Potential</p> <p>Plateau phase - Initiates trailing contraction</p> <p>Action potential</p> <p>Trailing contraction</p> <p>Leading contraction</p> <p>R B88</p>																								

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<p>B89</p>	<p>Amount of Acetylcholine Determines Amplitude of Plateau Phase of Action Potential and Contraction</p>	<p>Amount of Acetylcholine Determines Amplitude of Plateau Phase of Action Potential and Contraction</p>  <p>Excitatory muscolomotor neuron Acetylcholine release Antral muscle</p> <p>Plateau phase Gastric action potential Antral contraction</p> <p>More ACh release Intermediate release No ACh release</p> <p>R B89</p>
<p>B90</p>	<p>Jet-Like Retropropulsion Through the Orifice of the Antral Contraction Triturates Solid Particles</p>	<p>Jet-Like Retropropulsion Through the Orifice of the Antral Contraction Triturates Solid Particles</p>  <p>Antral contraction</p> <p>R B90</p>
<p>B91</p>	<p>Onset and Rate of Gastric Emptying Varies With the Composition of the Meal</p>	<p>Onset and Rate of Gastric Emptying Varies With the Composition of the Meal</p>  <p>Lag phase Emptying phase</p> <p>% Meal remaining in stomach</p> <p>Solid meal Semisolid meal Liquid meal</p> <p>Time after meal (min)</p> <p>R B91</p>

<p>B92</p>	<p>Dysmotility of the Stomach Reported in Functional Dyspepsia</p>	<p>Dysmotility of the Stomach Reported in Functional Dyspepsia</p>  <p>Abnormal antrofundic reflexes and intragastric distribution of food</p> <p>Antral dilatation</p> <p>Postprandial antral hypomotility</p> <p>Altered duodenal contractions</p> <p>Impaired adaptive relaxation of gastric reservoir</p> <p>Postprandial gastric dysrhythmias</p> <p>Delayed gastric emptying (solid > liquid)</p> <p>R</p> <p>B92</p>
<p>B93</p>	<p>Functional Dyspepsia: Putative Pathophysiological Mechanisms According to Predominant Symptom</p>	<p>Functional Dyspepsia: Putative Pathophysiological Mechanisms According to Predominant Symptom</p>  <p>Considerable overlap between predominant symptom subgroups</p> <p>Prevalence (% patients)</p> <p>90</p> <p>60</p> <p>30</p> <p>0</p> <p>Belching</p> <p>Bloating</p> <p>Early satiety</p> <p>Epigastric burning</p> <p>Postprandial fullness</p> <p>Epigastric pain</p> <p>Pain</p> <p>Vomiting</p> <p>Delayed solid emptying</p> <p>Hypersensitivity to gastric distension</p> <p>Impaired accommodation</p> <p><i>H. pylori</i> infection</p> <p>720 FD patients</p> <p>Impaired accommodation in ~80% of patients with pred. early satiety</p> <p>$P < 0.05$</p> <p>Karamanolis G et al. <i>Gastroenterology</i> 2006; 130:296</p> <p>R</p> <p>B93</p>
<p>B94</p>	<p>Gastric Reflexes in Functional Dyspepsia: Impaired Fundic, But Not Antral, Relaxation Occurs in Response to distension and Nutrients</p>	<p>Gastric Reflexes in Functional Dyspepsia: Impaired Fundic, But Not Antral, Relaxation Occurs in Response to distension and Nutrients</p>  <p>Antrofundic reflex</p> <p>Duodenofundic reflex</p> <p>Duodeno-antral reflex</p> <p>Fundic or antral reflex relaxation (ml)</p> <p>-100</p> <p>0</p> <p>200</p> <p>Functional dyspepsia</p> <ul style="list-style-type: none"> ● Ulcer-like ● Dysmotility-like ▲ Health <p>— Mean ± SE</p> <p>* $P < 0.05$ vs health</p> <p>Caldarella MP et al. <i>Gastroenterology</i> 2003; 124:1220</p> <p>R</p> <p>B94</p>

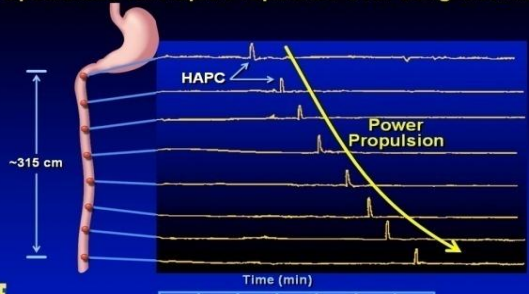
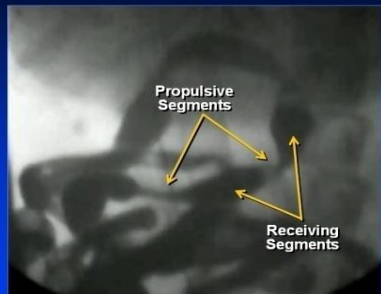
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B95	Electrogastrography: Noninvasive Recording of Gastric Antral Electrical Activity	 <p>Electrogastrography: Noninvasive Recording of Gastric Antral Electrical Activity</p> <p>Electrodes on abdominal surface</p> <p>Electrogastrogram</p> <p>2 min</p> <p>B95</p> <p>Detailed description: This slide shows a human torso with three electrodes placed on the abdominal surface. To the right, an 'Electrogastrogram' displays three distinct, regular, periodic waveforms. A scale bar below the waveforms indicates a duration of 2 minutes. A small 'R' logo is in the bottom left corner.</p>
B96	Tachygastria and Bradygastria Are Dysrhythmias Detected by Electrogastrography	 <p>Tachygastria and Bradygastria Are Dysrhythmias Detected by Electrogastrography</p> <p>Tachygastria Normal rhythm 3 cpm Bradygastria</p> <p>Frequency (cpm)</p> <p>B96</p> <p>Detailed description: This slide compares three types of gastric electrical activity. It features three 3D surface plots. The first plot, labeled 'Tachygastria', shows a high-frequency, irregular activity. The second plot, labeled 'Normal rhythm 3 cpm', shows a regular, low-frequency activity. The third plot, labeled 'Bradycardia', shows a low-frequency, irregular activity. Each plot has a horizontal axis labeled 'Frequency (cpm)' with markers at 2, 4, 6, and 8. A small 'R' logo is in the bottom left corner.</p>
B97	Section Title: Regional Motility – Small Intestine	
B98	The Migrating Motor Complex (MMC) Is the Gastric and Small-Intestinal Motor Pattern of the Interdigestive State	 <p>The Migrating Motor Complex (MMC) Is the Gastric and Small-Intestinal Motor Pattern of the Interdigestive State</p> <p>Manometric recording ports on catheter</p> <p>Time (min)</p> <p>MMC phase-III activity front</p> <p>B98</p> <p>Detailed description: This slide illustrates the Migrating Motor Complex (MMC) in the small intestine. On the left, a diagram of the small intestine shows several 'Manometric recording ports on catheter' placed at different points. On the right, a graph shows the resulting manometric recordings over time. The x-axis is labeled 'Time (min)' with markers at 0, 5, 10, 15, 20, and 25. The graph shows a series of waves that migrate down the intestine over time. A white arrow points to the 'MMC phase-III activity front', which is the most intense part of the complex. A small 'R' logo is in the bottom left corner.</p>



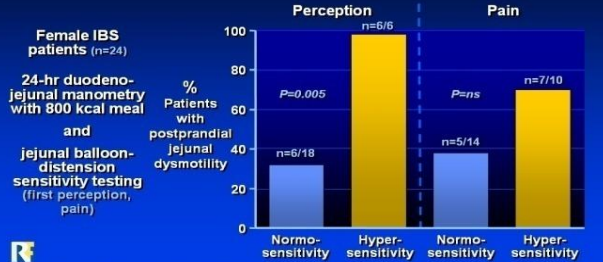
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<p>B99</p>	<p>The Migrating Motor Complex Occurs Periodically in the Interdigestive State in the Stomach and Small Intestine</p>	<p>The Migrating Motor Complex Occurs Periodically in the Interdigestive State in the Stomach and Small Intestine</p> <p>Phase I — Phase II — Phase III —</p> <p>Antrum Duodenum Jejunum Ileum</p> <p>0 1 2 3 4 5 6 Time (hrs)</p> <p>R B99</p>
<p>B100</p>	<p>Repetitive Cycles of Peristaltic Propulsion Occur Within the Migrating Activity Front of the MMC</p>	<p>Repetitive Cycles of Peristaltic Propulsion Occur Within the Migrating Activity Front of the MMC</p> <p>Maximum frequency of contractions in activity front (phase III) is that of electrical slow waves</p> <p>R B100</p>
<p>B101</p>	<p>Feeding Shifts Neural Programming From the Interdigestive Motility Pattern (MMC) to the Postprandial Pattern (Small-Bowel Segmentation)</p>	<p>Feeding Shifts Neural Programming From the Interdigestive Motility Pattern (MMC) to the Postprandial Pattern (Small-Bowel Segmentation)</p> <p>Interdigestive Meal ↓ Postprandial</p> <p>Segmenting motility Segmenting motility Segmenting motility Segmenting motility Segmenting motility</p> <p>Phase I — Phase II — Phase III —</p> <p>Antrum Duodenum Jejunum Ileum</p> <p>Time →</p> <p>R B101</p>

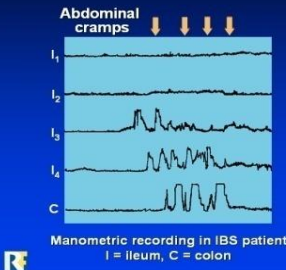
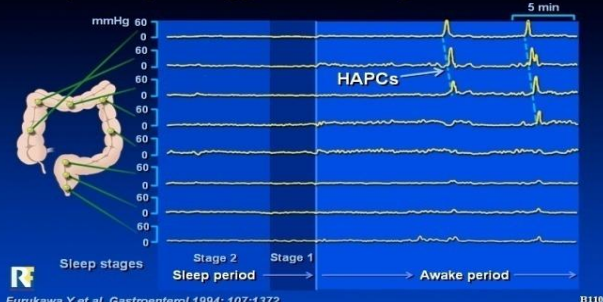
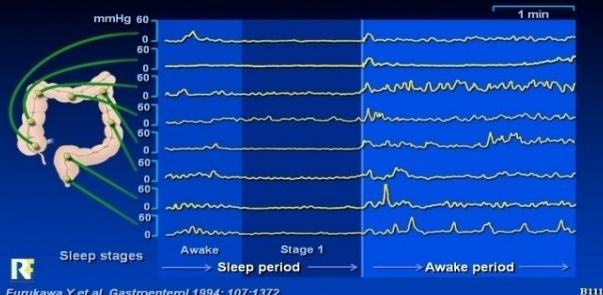
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<p>B102</p>	<p>Power Propulsion Is a Specialized Pattern of Intestinal Motility</p>	<p>Power Propulsion Is a Specialized Pattern of Intestinal Motility</p> <table border="1"> <thead> <tr> <th>Properties</th> <th>Functions</th> </tr> </thead> <tbody> <tr> <td> <ul style="list-style-type: none"> • High-amplitude propagated contraction (HAPC) • Rapid propagation • Long-distance propagation • Spike-triggered contraction • Unrelated to slow waves • Programmed by the ENS </td> <td> <ul style="list-style-type: none"> • Physiologic and defense, e.g., emesis • Rapid clearance • Clearance of long segments of intestine • Complements secretory defense mechanisms </td> </tr> </tbody> </table> <p>R B102</p>	Properties	Functions	<ul style="list-style-type: none"> • High-amplitude propagated contraction (HAPC) • Rapid propagation • Long-distance propagation • Spike-triggered contraction • Unrelated to slow waves • Programmed by the ENS 	<ul style="list-style-type: none"> • Physiologic and defense, e.g., emesis • Rapid clearance • Clearance of long segments of intestine • Complements secretory defense mechanisms
Properties	Functions					
<ul style="list-style-type: none"> • High-amplitude propagated contraction (HAPC) • Rapid propagation • Long-distance propagation • Spike-triggered contraction • Unrelated to slow waves • Programmed by the ENS 	<ul style="list-style-type: none"> • Physiologic and defense, e.g., emesis • Rapid clearance • Clearance of long segments of intestine • Complements secretory defense mechanisms 					
<p>B103</p>	<p>Power Propulsion Is an Intestinal Motor Pattern Specialized for Rapid Propulsion Over Long Distances</p>	<p>Power Propulsion Is an Intestinal Motor Pattern Specialized for Rapid Propulsion Over Long Distances</p>  <p>R B103</p>				
<p>B104</p>	<p>Emesis Interrupts the ENS Postprandial Program and Initiates Power-Propulsion Program</p>	<p>Emesis Interrupts the ENS Postprandial Program and Initiates Power-Propulsion Program</p> <p>Postprandial Mixing Program (Canine)</p> <p>Induction of emesis by apomorphine</p>  <p>R B104</p>				

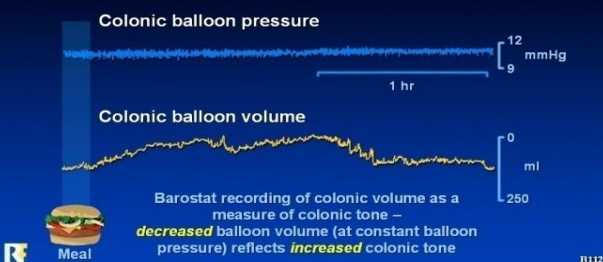
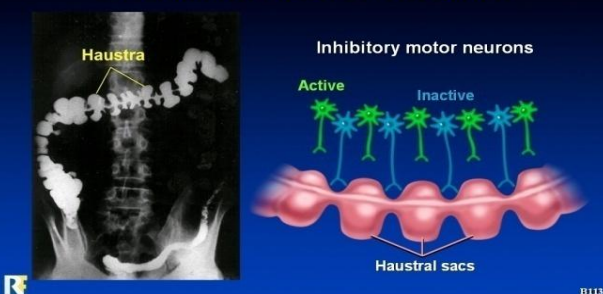
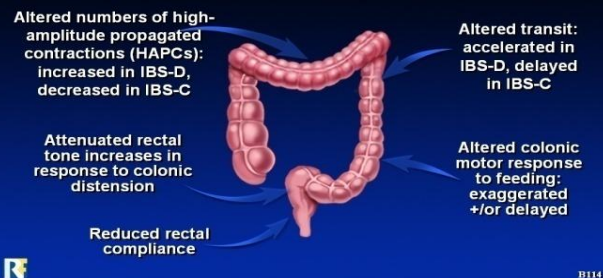
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<p>B105</p>	<p>Video: Emesis Interrupts the ENS Postprandial Program and Initiates Power-Propulsion Program</p>	<p>Emesis Interrupts the ENS Postprandial Program and Initiates Power-Propulsion Program</p>  <p>© Ehrlein - University of Hohenheim Courtesy of Hans Jurgen Ehrlein, DVM</p> <p>B105</p>									
<p>B106</p>	<p>Dysmotility of the Small Intestine Reported in Irritable Bowel Syndrome</p>	<p>Dysmotility of the Small Intestine Reported in Irritable Bowel Syndrome</p>  <ul style="list-style-type: none"> Abnormal propagation pattern of duodenal contractions Impaired segmental gas handling Increase in high-amplitude propagated contractions in ileum especially postprandially, CCK Subtle alterations in jejunal MMC: <ul style="list-style-type: none"> Phase 3 periodicity and amplitude Phase 2 duration and pattern Postprandial duration and pattern Alterations in transit <p>B106</p>									
<p>B107</p>	<p>Postprandial Jejunal Dysmotility Is More Frequent in IBS Patients with Jejunal Perception Hypersensitivity</p>	<p>Postprandial Jejunal Dysmotility Is More Frequent in IBS Patients With Jejunal Perception Hypersensitivity</p>  <p>Female IBS patients (n=24)</p> <p>24-hr duodeno-jejunal manometry with 800 kcal meal and jejunal balloon-distension sensitivity testing (first perception, pain)</p> <table border="1"> <thead> <tr> <th>Category</th> <th>Normo-sensitivity</th> <th>Hyper-sensitivity</th> </tr> </thead> <tbody> <tr> <td>Perception</td> <td>n=6/18</td> <td>n=6/6</td> </tr> <tr> <td>Pain</td> <td>n=5/14</td> <td>n=7/10</td> </tr> </tbody> </table> <p>Evans P et al. Gastroenterology 1996; 110:393</p> <p>B107</p>	Category	Normo-sensitivity	Hyper-sensitivity	Perception	n=6/18	n=6/6	Pain	n=5/14	n=7/10
Category	Normo-sensitivity	Hyper-sensitivity									
Perception	n=6/18	n=6/6									
Pain	n=5/14	n=7/10									

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<p>B108</p>	<p>High Amplitude Propagated Contractions in Ileum Reflect Power Propulsion</p>	<p>High-Amplitude Propagated Contractions in Ileum Reflect Power Propulsion</p>  <p>Abdominal cramps ↓ ↓ ↓</p> <p>I₁ I₂ I₃ I₄ C</p> <p>Manometric recording in IBS patient I = Ileum, C = colon</p> <ul style="list-style-type: none"> • Occur normally in ileum, stimulated by food, CCK, bile acids, short-chain fatty acids, etc. • Peristaltic, clear material refluxed from cecum • More common in IBS • Correlate with abdominal pain in some IBS patients <p>R B108</p>
<p>B109</p>	<p>Section Title: Regional Motility: Large Intestine/Pelvic Floor</p>	
<p>B110</p>	<p>Colonic Motility: High-Amplitude Propagated Contractions (HPACs) Are Triggered on Waking From Sleep</p>	<p>Colonic Motility: High-Amplitude Propagated Contractions (HPACs) Are Triggered on Waking From Sleep</p>  <p>mmHg 60 0 60 0 60 0 60 0 60 0 60 0</p> <p>HAPCs</p> <p>5 min</p> <p>Sleep stages Stage 2 Stage 1 Sleep period Awake period</p> <p>R <i>Furukawa Y et al. Gastroenterol 1994; 107:1372</i> B110</p>
<p>B111</p>	<p>Colonic Motility: Nonpropagating Contractions Decrease During Sleep and Increase on Waking</p>	<p>Colonic Motility: Nonpropagating Contractions Decrease During Sleep and Increase on Waking</p>  <p>mmHg 60 0 60 0 60 0 60 0 60 0 60 0</p> <p>1 min</p> <p>Sleep stages Awake Stage 1 Sleep period Awake period</p> <p>R <i>Furukawa Y et al. Gastroenterol 1994; 107:1372</i> B111</p>

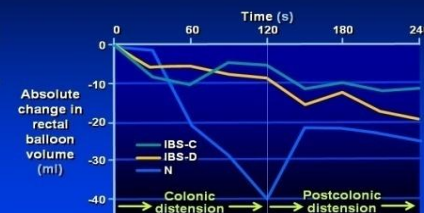

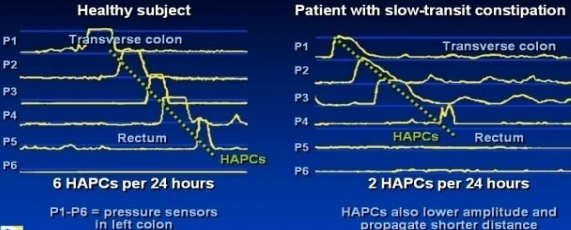
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<p>B112</p>	<p>Colonic Motility: Normal Tonic Response of Sigmoid Colon to a Meal</p>	<p>Colonic Motility: Normal Tonic Response of Sigmoid Colon to a Meal</p>  <p>Colonic balloon pressure</p> <p>Colonic balloon volume</p> <p>Barostat recording of colonic volume as a measure of colonic tone – decreased balloon volume (at constant balloon pressure) reflects increased colonic tone</p> <p>Meal</p> <p>B112</p>
<p>B113</p>	<p>Activity of Inhibitory Neurons is Important for Generation of Haustra in the Colon</p>	<p>Activity of Inhibitory Neurons Is Important for Generation of Haustra in the Colon</p>  <p>Haustra</p> <p>Inhibitory motor neurons</p> <p>Active Inactive</p> <p>Haustral sacs</p> <p>B113</p>
<p>B114</p>	<p>Dysmotility of the Colon Reported in Irritable Bowel Syndrome</p>	<p>Dysmotility of the Colon Reported in Irritable Bowel Syndrome</p>  <p>Altered numbers of high-amplitude propagated contractions (HAPCs): increased in IBS-D, decreased in IBS-C</p> <p>Altered transit: accelerated in IBS-D, delayed in IBS-C</p> <p>Attenuated rectal tone increases in response to colonic distension</p> <p>Altered colonic motor response to feeding: exaggerated +/- or delayed</p> <p>Reduced rectal compliance</p> <p>B114</p>

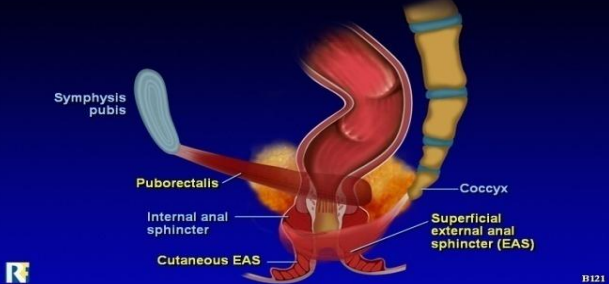
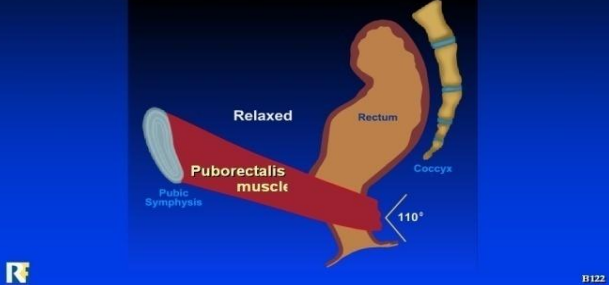
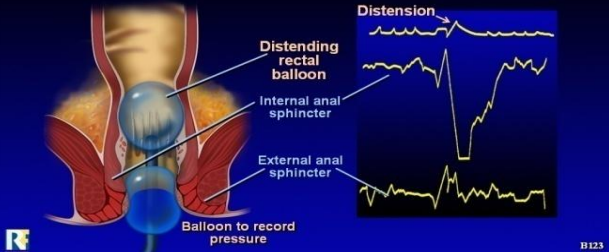
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<p>B115</p>	<p>Sigmoid Colon Motility Is Increased in IBS Both Fasting and Postprandially</p>	<p>Sigmoid Colon Motility Is Increased in IBS Both Fasting and Postprandially</p> <p>Motility index (AUC, mmHg)</p> <p>Health IBS</p> <p>Fasting Postprandial</p> <p>$P < 0.05$ vs fasting **</p> <p>$P < 0.05$ vs health *</p> <p>* $P < 0.05$ vs health and fasting **</p> <p>Houghton LA et al. <i>Neurogastroenterol Motil</i> 2007; 19:724</p> <p>B115</p>
<p>B116</p>	<p>Postprandial Sigmoid Colon Motility Index is Related to Plasma 5-HT Concentration in IBS</p>	<p>Postprandial Sigmoid Colon Motility Index Is Related to Plasma 5-HT Concentration in IBS</p> <p>Postprandial motility index (AUC, mmHg)</p> <p>Postprandial platelet-depleted plasma 5-HT concentration (nmol/L)</p> <p>• IBS ▲ Health</p> <p>IBS: $r = 0.435$; $P = 0.009$ Health: $r = 0.338$; $P = 0.201$</p> <p>Houghton LA et al. <i>Neurogastroenterol Motil</i> 2007; 19:724</p> <p>B116</p>
<p>B117</p>	<p>Power Propulsion in the Colon is More Frequent in IBS</p>	<p>Power Propulsion in the Colon Is More Frequent in IBS</p> <p>High-amplitude propagated contractions (no./hour)</p> <p>Amplitude of contraction (mmHg)</p> <p>Fasting Meal Cholecystokinin</p> <p>Health IBS</p> <p>Chey WY et al. <i>Am J Gastroenterol</i> 2001; 96:1499</p> <p>B117</p>

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<p>B118</p>	<p>The Normal Colorectal Tonic Reflex Is Attenuated in Female IBS Patients</p>	<p>The Normal Colorectal Tonic Reflex Is Attenuated in Female IBS Patients</p> <p>Colonic and rectal barostat balloons, 2-min descending-colon phasic distension, concurrent rectal balloon volume</p> <p>8 IBS - constipation 8 IBS - diarrhea 8 healthy subjects</p>  <p>The graph plots 'Absolute change in rectal balloon volume (ml)' on the y-axis (from 0 to -40) against 'Time (s)' on the x-axis (from 0 to 240). Three lines represent different groups: IBS-C (blue), IBS-D (orange), and N (green). The x-axis is divided into 'Colonic distension' (0-120s) and 'Postcolonic distension' (120-240s). All groups show a decrease in volume during colonic distension. The N group shows a sharp drop to approximately -35 ml during colonic distension, followed by a recovery to about -15 ml during postcolonic distension. The IBS-C group shows a smaller drop to about -15 ml during colonic distension and recovers to about -10 ml. The IBS-D group shows a drop to about -10 ml during colonic distension and recovers to about -5 ml. The legend indicates: IBS-C (blue line), IBS-D (orange line), N (green line).</p> <p>Ng C et al. Am J Physiol 2005; 289:4894</p> <p>B118</p>
<p>B119</p>	<p>Dysmotility of the Colon and Ano-Rectum Reported in Functional Constipation</p>	<p>Dysmotility of the Colon and Anorectum Reported in Functional Constipation</p>  <p>Reduced/absent high-amplitude propagated contractions (HAPCs)</p> <p>Delayed transit: segmental, generalized</p> <p>Impairment of normal low-amplitude contractile activity</p> <p>Attenuated motor response to meals and to waking</p> <p>Dyssynergic defecation, inadequate defecatory propulsion</p> <p>Absence of normal predefecatory propagating sequences</p> <p>B119</p>
<p>B120</p>	<p>High-Amplitude Propagated Contractions (HAPCs) Occur Less Frequently in Slow-Transit Constipation</p>	<p>High-Amplitude Propagated Contractions (HAPCs) Occur Less Frequently in Slow-Transit Constipation</p>  <p>The figure compares pressure sensor traces for a 'Healthy subject' and a 'Patient with slow-transit constipation'. The healthy subject's traces (P1-P6) show frequent, high-amplitude propagated contractions (HAPCs) that propagate from the transverse colon (P1) to the rectum (P6). The patient's traces show fewer and lower-amplitude HAPCs that propagate a shorter distance. The legend indicates: P1-P6 = pressure sensors in left colon.</p> <p>6 HAPCs per 24 hours</p> <p>2 HAPCs per 24 hours</p> <p>HAPCs also lower amplitude and propagate shorter distance</p> <p>Rao SC et al. Am J Gastroenterol 2004; 99:2405</p> <p>B120</p>

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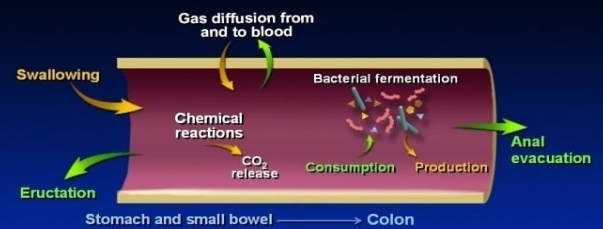
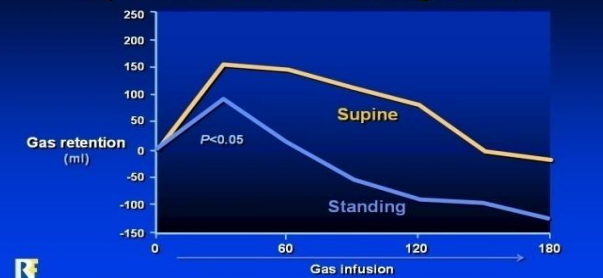
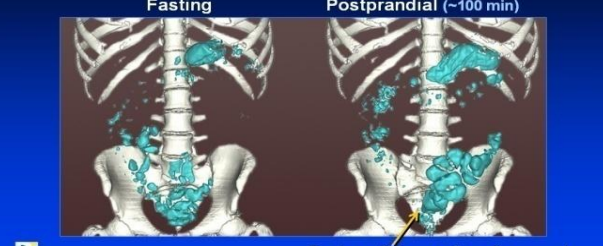
B121	External Anal Sphincter and Puborectalis Are Skeletal Muscles Under Spinal Motor Control	<p>External Anal Sphincter and Puborectalis Are Skeletal Muscles Under Spinal Motor Control</p> 
B122	The Anorectal Angle Is Determined by the Contractile State of the Puborectalis Muscle	<p>The Anorectal Angle Is Determined by the Contractile State of the Puborectalis Muscle</p> 
B123	Balloon Distension in the Rectum Normally Evokes Relaxation of the External Anal Sphincter	<p>Balloon Distension in the Rectum Normally Evokes Relaxation of the External Anal Sphincter</p> 

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<p>B124</p>	<p>Colonic Motility: Nonpropagating Contractions Decrease During Sleep and Increase on Waking</p>	<p>Colonic Motility: Nonpropagating Contractions Decrease During Sleep and Increase on Waking</p> <p>mmHg 60 0 60 0 60 0 60 0 60 0 60 0</p> <p>1 min</p> <p>Sleep stages Awake → Sleep period → Awake period</p> <p>Furukawa Y et al. Gastroenterol 1994; 107:1372</p> <p>B124</p>
<p>B125</p>	<p>Patterns of Anal Sphincter Dysfunction</p>	<p>Patterns of Anal Sphincter Dysfunction</p> <p>Health Spinal cord injury Hirschsprung's disease</p> <p>Distension Internal anal sphincter External anal sphincter</p> <p>Distension Internal anal sphincter External anal sphincter</p> <p>Distension Internal anal sphincter External anal sphincter</p> <p>B125</p>
<p>B126</p>	<p>Genetic Factors May Modulate Adrenergic and Serotonergic Functions in IBS</p>	<p>Genetic Factors May Modulate Adrenergic and Serotonergic Functions in IBS</p> <p>90 IBS-constipation patients</p> <p>Significant association between phenotype of IBS-constipation and an α_2 adrenoceptor polymorphism (OR = 2.48)</p> <p>This same polymorphism, alone or combined with a serotonin transporter polymorphism, also significantly associated with a high somatic symptom score</p> <p>SLC 6A4 + α_{2A}-1291 (C → G)</p> <p>SLC 6A4 + α_{2C}Del 322-325</p> <p>α_{2C}Del 322-325 P=0.05</p> <p>α_{2A}-1291 (C → G) P=0.08</p> <p>SLC 6A4</p> <p>0 2 4 6 8 10 12 14</p> <p>Odds ratio (95% CI)</p> <p>Kim HJ et al. Gut 2004; 53:829</p> <p>B126</p>
<p>B127</p>	<p>Section Title: Intestinal Bacteria, Intestinal Gas, Abdominal Bloating, and Distension</p>	

<p>B128</p>	<p>The Microbiota of the Human GI Tract</p>	<p>The Microbiota of the Human GI Tract</p> <ul style="list-style-type: none"> • Complex ecosystem of 10^{14} bacterial cells • Majority of species not cultivable • Vital for development of host immune system • Functions as a barrier against pathogens • Appears capable of signaling to enterochromaffin cells and neurons to influence motility and sensitivity <p>R</p> <p>B128</p>																					
<p>B129</p>	<p>Alterations in Intestinal Microflora May Occur in IBS</p>	<p>Alterations in Intestinal Microflora May Occur in IBS</p> <ul style="list-style-type: none"> • Abnormal colonic fermentation in IBS, e.g., increased hydrogen production (King, 1998) • Quantitative alterations in GI microbiota (Balsari, 1982; Si, 2004), and related to predominant bowel habit, e.g., <ul style="list-style-type: none"> ↓ <i>Lactobacillus</i> species in IBS - diarrhea ↑ <i>Veillonella</i> species in IBS - constipation (Malinen, 2005) • Significant differences between microbiota in IBS and in health have been confirmed using more sophisticated molecular characterization (Kassinen, 2007) • Further studies are required in large, community-based IBS patient samples <p>R</p> <p>B129</p>																					
<p>B130</p>	<p>Mild Increases of Small-Bowel Bacteria, but Not Overgrowth, Can Occur in IBS Patients</p>	<p>Mild Increases of Small-Bowel Bacteria, but Not Overgrowth, Can Occur in IBS Patients</p> <table border="1"> <caption>Approximate data from the bar chart</caption> <thead> <tr> <th>Parameter</th> <th>IBS (n=162) (%)</th> <th>Healthy subjects (n=42) (%)</th> </tr> </thead> <tbody> <tr> <td><math>< 5000</math> cfu/ml</td> <td>~45</td> <td>~10</td> </tr> <tr> <td>>=100,000 cfu/ml (small-bowel bacterial overgrowth)</td> <td>~10</td> <td>~5</td> </tr> <tr> <td>GHBT</td> <td>~15</td> <td>~5</td> </tr> <tr> <td>LHBT double peak</td> <td>~20</td> <td>~10</td> </tr> <tr> <td>LHBT 90 min</td> <td>~40</td> <td>~15</td> </tr> <tr> <td>LHBT 180 min</td> <td>~75</td> <td>~65</td> </tr> </tbody> </table> <p>R</p> <p>Posserud J et al. Gut. 2007; 56: 802</p> <p>B130</p>	Parameter	IBS (n=162) (%)	Healthy subjects (n=42) (%)	<math>< 5000</math> cfu/ml	~45	~10	>=100,000 cfu/ml (small-bowel bacterial overgrowth)	~10	~5	GHBT	~15	~5	LHBT double peak	~20	~10	LHBT 90 min	~40	~15	LHBT 180 min	~75	~65
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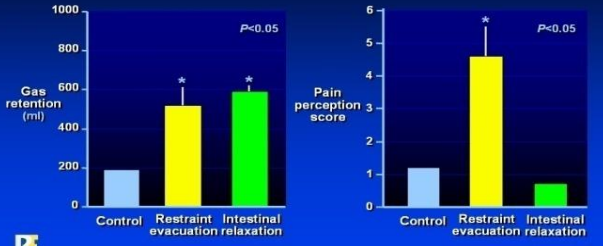
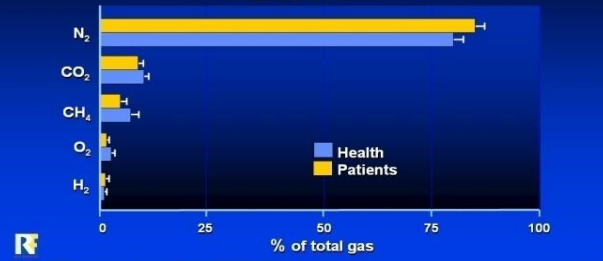
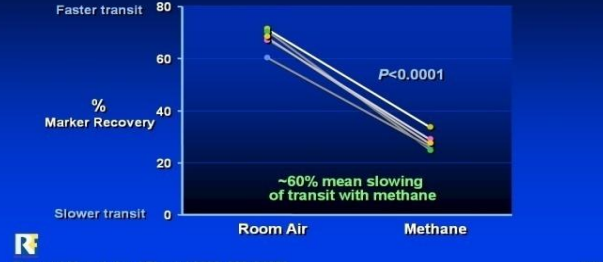
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<p>B131</p>	<p>Normal Intestinal Gas Dynamics Balance Gas Production and Gas Elimination</p>	<p>Normal Intestinal Gas Dynamics Balance Gas Production and Gas Elimination</p>  <p>Swallowing → Stomach and small bowel → Colon → Anal evacuation</p> <p>Gas diffusion from and to blood</p> <p>Chemical reactions → CO₂ release</p> <p>Bacterial fermentation → Consumption → Production</p> <p>Eructation</p> <p>Total volume of intraluminal gas only ~ 100-200 ml</p> <p><small>Adapted from Azpiroz F, Malagelada J-R. Gastroenterology 2005; 129:1060</small></p> <p>B131</p>
<p>B132</p>	<p>Intestinal Gas Retention Occurs in the Supine but Not in the Standing Position</p>	<p>Intestinal Gas Retention Occurs in the Supine but Not in the Standing Position</p>  <p>Gas retention (ml)</p> <p>Gas Infusion (min)</p> <p>Supine</p> <p>Standing</p> <p>$P < 0.05$</p> <p><small>Dalnesi R et al. Gut. 2003; 52:969</small></p> <p>B132</p>
<p>B133</p>	<p>Distribution of Abdominal Gas on CT Scans Before and After Meal Ingestion in a Healthy Subject</p>	<p>Distribution of Abdominal Gas on CT Scans Before and After Meal Ingestion in a Healthy Subject</p>  <p>Fasting</p> <p>Postprandial (~100 min)</p> <p>Postprandial gas volume increment occurs in distal colon</p> <p><small>Perez F et al. Am J Gastroenterol 2007; 102:842</small></p> <p>B133</p>

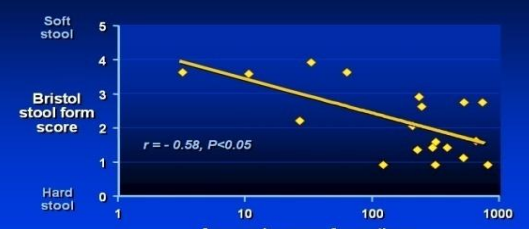
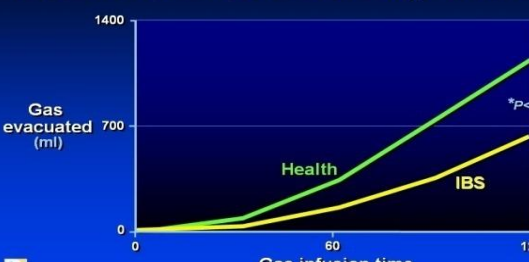
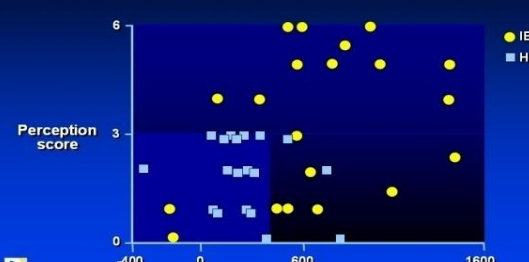
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<p>B134</p>	<p>Abdominal Distension in IBS Increases During the Day and Decreases at Night</p>	<p>Abdominal Distension in IBS Increases During the Day and Decreases at Night</p> <table border="1"> <caption>Abdominal girth (cm) data</caption> <thead> <tr> <th>Group</th> <th>Beginning day 1</th> <th>End day 1</th> <th>Beginning day 2</th> </tr> </thead> <tbody> <tr> <td>IBS-diarrhea</td> <td>~85</td> <td>~88</td> <td>~84</td> </tr> <tr> <td>IBS-constipation</td> <td>~84</td> <td>~88</td> <td>~83</td> </tr> <tr> <td>Health</td> <td>~84</td> <td>~83</td> <td>~82</td> </tr> </tbody> </table> <p><i>Houghton LA et al. Gastroenterology 2006; 131:1003</i></p>	Group	Beginning day 1	End day 1	Beginning day 2	IBS-diarrhea	~85	~88	~84	IBS-constipation	~84	~88	~83	Health	~84	~83	~82
Group	Beginning day 1	End day 1	Beginning day 2															
IBS-diarrhea	~85	~88	~84															
IBS-constipation	~84	~88	~83															
Health	~84	~83	~82															
<p>B135</p>	<p>Mild Exercise Enhances Transit of Intestinal Gas</p>	<p>Mild Exercise Enhances Transit of Intestinal Gas</p> <table border="1"> <caption>Gas retention (ml) and Abdominal distension (mm) data</caption> <thead> <tr> <th>Condition</th> <th>Gas retention (ml)</th> <th>Abdominal distension (mm)</th> </tr> </thead> <tbody> <tr> <td>Rest</td> <td>~100</td> <td>~8</td> </tr> <tr> <td>Exercise</td> <td>~-100</td> <td>~3</td> </tr> </tbody> </table> <p><i>Dainese R et al. Am J Med 2004; 116:536</i></p>	Condition	Gas retention (ml)	Abdominal distension (mm)	Rest	~100	~8	Exercise	~-100	~3							
Condition	Gas retention (ml)	Abdominal distension (mm)																
Rest	~100	~8																
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<p>B136</p>	<p>Tolerance is Less for Jejunal Than for Colonic Gas Infusion</p>	<p>Tolerance is Less for Jejunal Than for Colonic Gas Infusion</p> <table border="1"> <caption>Subjective perception score and Abdominal distension (mm) data</caption> <thead> <tr> <th>Location</th> <th>Subjective perception score</th> <th>Abdominal distension (mm)</th> </tr> </thead> <tbody> <tr> <td>Jejunum</td> <td>~4.5</td> <td>~14</td> </tr> <tr> <td>Colon</td> <td>~1.5</td> <td>~13</td> </tr> </tbody> </table> <p><i>Harder H et al. Gut 2003; 52:1708</i></p>	Location	Subjective perception score	Abdominal distension (mm)	Jejunum	~4.5	~14	Colon	~1.5	~13							
Location	Subjective perception score	Abdominal distension (mm)																
Jejunum	~4.5	~14																
Colon	~1.5	~13																

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<p>B137</p>	<p>Gas Retention Due to Intestinal Relaxation Is Better Tolerated Than Retention Due to Restraint Evacuation</p>	<p>Gas Retention Due to Intestinal Relaxation Is Better Tolerated Than Retention Due to Restraint Evacuation</p>  <p>Gas retention (ml)</p> <table border="1"> <thead> <tr> <th>Condition</th> <th>Gas retention (ml)</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>~180</td> </tr> <tr> <td>Restraint evacuation</td> <td>~500*</td> </tr> <tr> <td>Intestinal relaxation</td> <td>~580*</td> </tr> </tbody> </table> <p>Pain perception score</p> <table border="1"> <thead> <tr> <th>Condition</th> <th>Pain perception score</th> </tr> </thead> <tbody> <tr> <td>Control</td> <td>~1.2</td> </tr> <tr> <td>Restraint evacuation</td> <td>~4.5*</td> </tr> <tr> <td>Intestinal relaxation</td> <td>~0.8</td> </tr> </tbody> </table> <p>Serra J et al. Am J Physiol 2001; 281:G138</p> <p>B137</p>	Condition	Gas retention (ml)	Control	~180	Restraint evacuation	~500*	Intestinal relaxation	~580*	Condition	Pain perception score	Control	~1.2	Restraint evacuation	~4.5*	Intestinal relaxation	~0.8		
Condition	Gas retention (ml)																			
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Restraint evacuation	~4.5*																			
Intestinal relaxation	~0.8																			
<p>B138</p>	<p>Composition of Intestinal Gas Is Not Different in Healthy Subjects and Patients with Functional GI Symptoms</p>	<p>Composition of Intestinal Gas Is Not Different in Healthy Subjects and Patients with Functional GI Symptoms</p>  <table border="1"> <thead> <tr> <th>Gas</th> <th>Health (%)</th> <th>Patients (%)</th> </tr> </thead> <tbody> <tr> <td>N₂</td> <td>~85</td> <td>~85</td> </tr> <tr> <td>CO₂</td> <td>~10</td> <td>~10</td> </tr> <tr> <td>CH₄</td> <td>~5</td> <td>~5</td> </tr> <tr> <td>O₂</td> <td>~1</td> <td>~1</td> </tr> <tr> <td>H₂</td> <td>~1</td> <td>~1</td> </tr> </tbody> </table> <p>Lasser RB et al. New Engl J Med 1975; 293:524</p> <p>B138</p>	Gas	Health (%)	Patients (%)	N ₂	~85	~85	CO ₂	~10	~10	CH ₄	~5	~5	O ₂	~1	~1	H ₂	~1	~1
Gas	Health (%)	Patients (%)																		
N ₂	~85	~85																		
CO ₂	~10	~10																		
CH ₄	~5	~5																		
O ₂	~1	~1																		
H ₂	~1	~1																		
<p>B139</p>	<p>Methane Infusion Into the Canine Distal Small Bowel Slows Transit in the Proximal Small Bowel</p>	<p>Methane Infusion Into the Canine Distal Small Bowel Slows Transit in the Proximal Small Bowel</p>  <table border="1"> <thead> <tr> <th>Condition</th> <th>Room Air (%)</th> <th>Methane (%)</th> </tr> </thead> <tbody> <tr> <td>Marker Recovery</td> <td>~60</td> <td>~25</td> </tr> </tbody> </table> <p>~60% mean slowing of transit with methane</p> <p>P < 0.0001</p> <p>Pimentel M et al. Am J Physiol 2006; 290:G1089</p> <p>B139</p>	Condition	Room Air (%)	Methane (%)	Marker Recovery	~60	~25												
Condition	Room Air (%)	Methane (%)																		
Marker Recovery	~60	~25																		

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<p>B140</p>	<p>The Degree of Breath Methane Production in IBS Correlates With Severity of Constipation</p>	<p>The Degree of Breath Methane Production in IBS Correlates With Severity of Constipation</p>  <p>$r = -0.58, P < 0.05$</p> <p>Chatterjee S et al. <i>Am J Gastroenterol</i> 2007; 102:837</p> <p>B140</p>
<p>B141</p>	<p>Evacuation of Intestinal Gas is Impaired in IBS</p>	<p>Evacuation of Intestinal Gas Is Impaired in IBS</p>  <p>*$P < 0.01$</p> <p>Serra J et al. <i>Gut</i> 2001; 48:14</p> <p>B141</p>
<p>B142</p>	<p>IBS Patients Exhibit Impaired Gas Transit Associated With Enhanced Perception</p>	<p>IBS Patients Exhibit Impaired Gas Transit Associated With Enhanced Perception</p>  <p>Perception score</p> <p>Gas retained (ml)</p> <p>● IBS ■ Health</p> <p>Serra J et al. <i>Gut</i> 2001; 48:14</p> <p>B142</p>

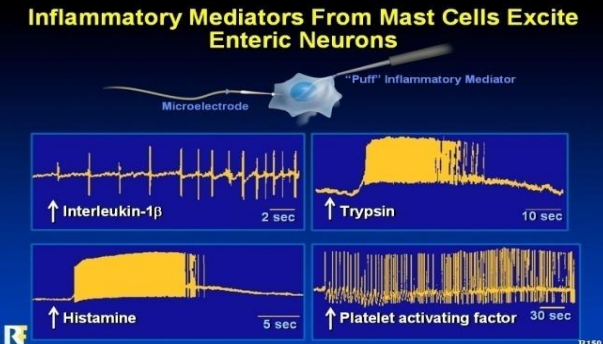
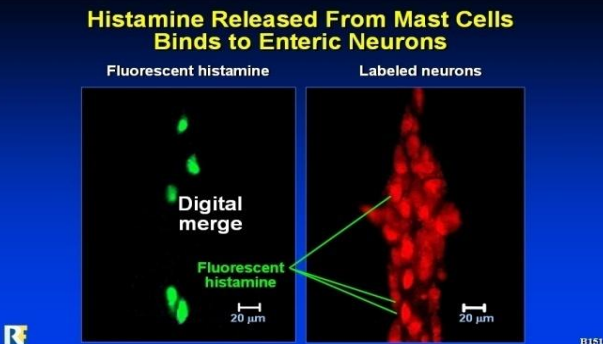
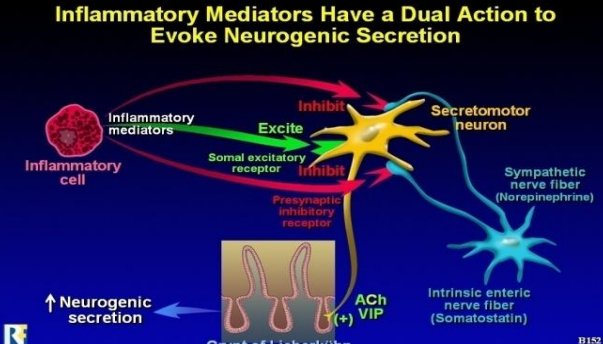
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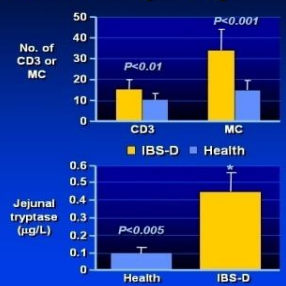
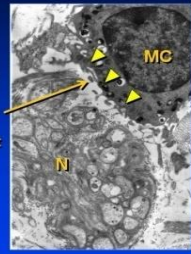
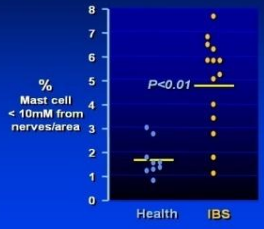
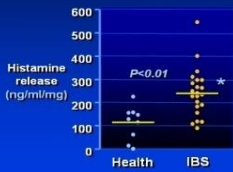
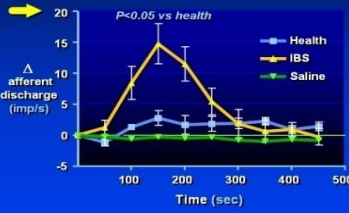
<p>B143</p>	<p>Impaired Intestinal Transit of Gas in Patients with Bloating Occurs in the Small Bowel</p>	<p>Impaired Intestinal Transit of Gas in Patients with Bloating Occurs in the Small Bowel</p> <p>Transit time (50% of gas)</p> <p>Small bowel + colon</p> <p>Small bowel</p> <p>Colon</p> <p>Health Patients with bloating</p> <p>Health Bloating</p> <p>Salvioli B et al. <i>Gastroenterology</i> 2005; 128:574</p> <p>B143</p>
<p>B144</p>	<p>Reflex Inhibition of Intestinal Gas Transit by Lipid Is Enhanced in IBS</p>	<p>Reflex Inhibition of Intestinal Gas Transit by Lipid Is Enhanced in IBS</p> <p>Gas retained (ml)</p> <p>Jejunal gas infusion (min)</p> <p>Lipids alone</p> <p>Lipids + rectal distension</p> <p>IBS patients</p> <p>Healthy subjects</p> <p>Passos MC et al. <i>Gut</i>. 2005; 54:344</p> <p>B144</p>
<p>B145</p>	<p>Patients With Functional Bloating Exhibit Impaired Abdominal Muscle Tone in Response to Colonic Gas Infusion</p>	<p>Patients With Functional Bloating Exhibit Impaired Abdominal Muscle Tone in Response to Colonic Gas Infusion</p> <p>Change in EMG activity (%)</p> <p>Upper rectus</p> <p>Lower rectus</p> <p>External oblique</p> <p>Internal oblique</p> <p>Health</p> <p>Functional bloating</p> <p>Tremolaterra F et al. <i>Gastroenterology</i> 2006; 130:1062</p> <p>B145</p>

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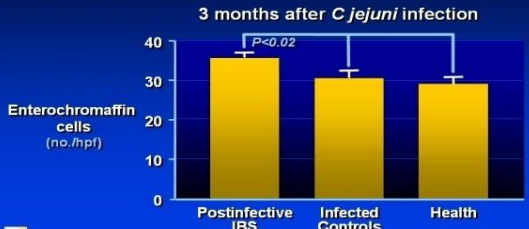
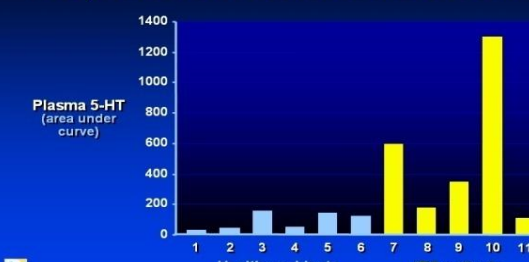
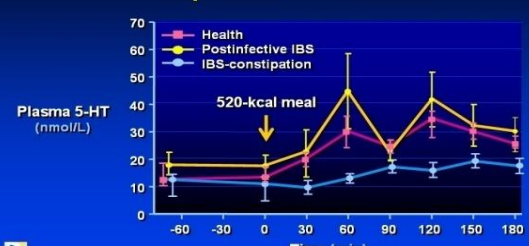
<p>B146</p>	<p>Functional Abdominal Bloating and Distension: Mechanistic Hypotheses</p>	<p>Functional Abdominal Bloating and Distension: Mechanistic Hypotheses</p> <p>Bloating: subjective sensation of abdominal fullness/gas</p> <p>Somatic perception</p> <p>Visceral hypersensitivity</p> <p>Distension: objective increase in abdominal girth</p> <p>Impaired viscerovisceral reflexes</p> <p>Increased intraluminal gas</p> <p>Impaired viscerosomatic reflexes</p> <p><small>Adapted from Azpiroz F, Malagelada J-R. Gastroenterology 2005; 129:1060</small></p> <p><small>B146</small></p>
<p>B147</p>	<p>Section Title: Stress, Inflammation, and Brain-Gut Interactions</p>	
<p>B148</p>	<p>Mast Cell Signaling: Intestinal Mast Cells Release Multiple Mediators</p>	<p>Mast Cell Signaling: Intestinal Mast Cells Release Multiple Mediators</p> <ul style="list-style-type: none"> • Chemoattractant factors <ul style="list-style-type: none"> • Immune/inflammatory • Paracrine signals to <ul style="list-style-type: none"> • enteric nervous system • sympathetic nerve terminals • sensory afferents <p><small>B148</small></p>
<p>B149</p>	<p>Sensory Afferents Express Receptors for Inflammatory Mediators</p>	<p>Sensory Afferents Express Receptors for Inflammatory Mediators</p> <p>Mechanoreceptor in series</p> <p>Inflammatory receptors</p> <p>Bradykinin Histamine Mast-cell tryptase</p> <p>Spinal afferent</p> <p>Enteric nervous system</p> <p>Sub P CGRP others</p> <p>Afferent fiber</p> <p>Dorsal root ganglion</p> <p>Sub P CGRP others</p> <p>Spinal cord</p> <p>CNS</p> <p><small>B149</small></p>

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<p>B150</p>	<p>Inflammatory Mediators From Mast Cells Excite Enteric Neurons</p>	<p>Inflammatory Mediators From Mast Cells Excite Enteric Neurons</p>  <p>Microelectrode "Puff" Inflammatory Mediator</p> <p>↑ Interleukin-1β 2 sec</p> <p>↑ Trypsin 10 sec</p> <p>↑ Histamine 5 sec</p> <p>↑ Platelet activating factor 30 sec</p> <p>B150</p>
<p>B151</p>	<p>Histamine Released From Mast Cells Binds to Enteric Neurons</p>	<p>Histamine Released From Mast Cells Binds to Enteric Neurons</p>  <p>Fluorescent histamine Labeled neurons</p> <p>Digital merge</p> <p>Fluorescent histamine</p> <p>20 μm</p> <p>20 μm</p> <p>B151</p>
<p>B152</p>	<p>Inflammatory Mediators Have a Dual Action to Evoke Neurogenic Secretion</p>	<p>Inflammatory Mediators Have a Dual Action to Evoke Neurogenic Secretion</p>  <p>Inflammatory cell</p> <p>Inflammatory mediators</p> <p>Excite</p> <p>Somal excitatory receptor</p> <p>Inhibit</p> <p>Presynaptic inhibitory receptor</p> <p>Secretomotor neuron</p> <p>Sympathetic nerve fiber (Norepinephrine)</p> <p>Intrinsic enteric nerve fiber (Somatostatin)</p> <p>↑ Neurogenic secretion</p> <p>ACh (+)</p> <p>VIP (+)</p> <p>Crypt of Lieberkühn</p> <p>B152</p>

<p>B153</p>	<p>Jejunal Mast Hyperplasia and Activation Is Present in IBS-Diarrhea Patients (IBS-D)</p>	<p>Jejunal Mast Hyperplasia and Activation Is Present in IBS-Diarrhea Patients (IBS-D)</p> <p>20 IBS-D and 14 healthy subjects underwent capsule jejunal biopsy</p> <p>In IBS</p> <ul style="list-style-type: none"> • ↑ intraepithelial lymphocytes (CD3 / 100 epithelial cells) and • ↑ mast cells (MC / hpf) • ↑ tryptase release from biopsy  <p><i>Gullarte M et al. Gut 2007; 56:203</i></p>
<p>B154</p>	<p>Mast Cells Infiltrate and Associate With Nerve Fibers in Colonic Mucosa of IBS Patients</p>	<p>Mast Cells Infiltrate and Associate With Nerve Fibers in Colonic Mucosa of IBS Patients</p>   <p><i>Barbara G et al. Gastroenterology 2007; 132:26</i></p>
<p>B155</p>	<p>Increased Mast Cell Mediators From Colonic Mucosa of IBS Patients Excite Rat Visceral Sensory Nerves</p>	<p>Increased Mast Cell Mediators From Colonic Mucosa of IBS Patients Excite Rat Visceral Sensory Nerves</p> <p>Increased histamine release from IBS colonic biopsies</p>  <p>Increased rat mesenteric afferent discharge from IBS (but not healthy) colonic biopsies supernatant</p>  <p><i>Barbara G et al. Gastroenterology 2007; 132:26</i></p>

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<p>B156</p>	<p>Patients With Postinfective IBS Exhibit Mucosal 5-HT-Containing Enterochromaffin Cell Hyperplasia</p>	<p>Patients With Postinfective IBS Exhibit Mucosal 5-HT-Containing Enterochromaffin Cell Hyperplasia</p> <p>3 months after <i>C jejuni</i> infection</p>  <table border="1"> <caption>Enterochromaffin cells (no./mpf)</caption> <thead> <tr> <th>Group</th> <th>Enterochromaffin cells (no./mpf)</th> </tr> </thead> <tbody> <tr> <td>Postinfective IBS</td> <td>~35</td> </tr> <tr> <td>Infected Controls</td> <td>~30</td> </tr> <tr> <td>Health</td> <td>~28</td> </tr> </tbody> </table> <p>Dunlop SP et al. <i>Gastroenterology</i> 2003; 125:1651</p> <p>B156</p>	Group	Enterochromaffin cells (no./mpf)	Postinfective IBS	~35	Infected Controls	~30	Health	~28																																
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<p>B157</p>	<p>Postprandial 5-HT Release Is Elevated in IBS</p>	<p>Postprandial 5-HT Release Is Elevated in IBS</p>  <table border="1"> <caption>Plasma 5-HT (area under curve)</caption> <thead> <tr> <th>Group</th> <th>Plasma 5-HT (area under curve)</th> </tr> </thead> <tbody> <tr> <td>Healthy subjects</td> <td>~100</td> </tr> <tr> <td>IBS patients</td> <td>~1300</td> </tr> </tbody> </table> <p>Beacroft CP et al. <i>Gut</i> 1998; 42:42</p> <p>B157</p>	Group	Plasma 5-HT (area under curve)	Healthy subjects	~100	IBS patients	~1300																																		
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<p>B158</p>	<p>IBS-Constipation Patients Show Impaired and Postinfective IBS Patients Show Enhanced Postprandial 5-HT Release</p>	<p>IBS-Constipation Patients Show Impaired, and Postinfective IBS Patients Show Enhanced Postprandial 5-HT Release</p>  <table border="1"> <caption>Plasma 5-HT (nmol/L) over time</caption> <thead> <tr> <th>Time (min)</th> <th>Health (nmol/L)</th> <th>Postinfective IBS (nmol/L)</th> <th>IBS-constipation (nmol/L)</th> </tr> </thead> <tbody> <tr> <td>-60</td> <td>~15</td> <td>~15</td> <td>~15</td> </tr> <tr> <td>-30</td> <td>~15</td> <td>~15</td> <td>~15</td> </tr> <tr> <td>0 (Meal)</td> <td>~15</td> <td>~15</td> <td>~15</td> </tr> <tr> <td>30</td> <td>~25</td> <td>~30</td> <td>~15</td> </tr> <tr> <td>60</td> <td>~35</td> <td>~45</td> <td>~15</td> </tr> <tr> <td>90</td> <td>~25</td> <td>~30</td> <td>~15</td> </tr> <tr> <td>120</td> <td>~35</td> <td>~45</td> <td>~15</td> </tr> <tr> <td>150</td> <td>~30</td> <td>~35</td> <td>~15</td> </tr> <tr> <td>180</td> <td>~25</td> <td>~30</td> <td>~15</td> </tr> </tbody> </table> <p>Dunlop SP et al. <i>Clin Gastroenterol Hepatol</i> 2005; 3:349</p> <p>B158</p>	Time (min)	Health (nmol/L)	Postinfective IBS (nmol/L)	IBS-constipation (nmol/L)	-60	~15	~15	~15	-30	~15	~15	~15	0 (Meal)	~15	~15	~15	30	~25	~30	~15	60	~35	~45	~15	90	~25	~30	~15	120	~35	~45	~15	150	~30	~35	~15	180	~25	~30	~15
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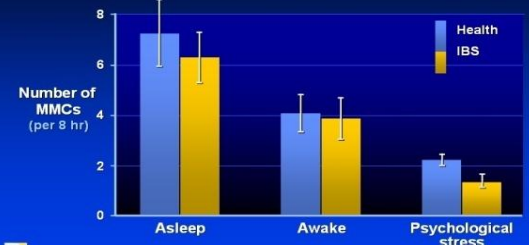

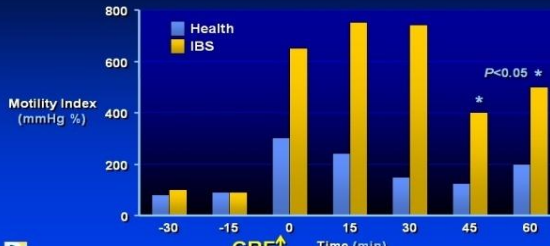
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<p>B159</p>	<p>Brain-Gut Interactions as a Consequence of Psychosocial Stress</p>	<p>Brain-Gut Interactions as a Consequence of Psychosocial Stress</p> <p>Mental stress</p> <p>Brain - mast cell connection</p> <p>Enteric nervous system • Defense program</p> <p>Paracrine mediators, e.g. histamine</p> <p>Intraluminal antigen</p> <p>Mast cell</p> <p>Chemoattractant factors</p> <p>Inflammatory surveillance</p> <p>Effector systems • Muscle • Secretory epithelium • Blood vessels</p> <p>Gut behavior power propulsion hypersecretion ↑ blood flow</p> <p>Symptoms diarrhea - pain</p> <p>B159</p>
<p>B160</p>	<p>Cold Water Stress or Antigen Challenge Leads to Degranulation of Enteric Mast Cells in Humans</p>	<p>Cold Water Stress or Antigen Challenge Leads to Degranulation of Enteric Mast Cells in Humans</p> <p>Mast cell tryptase release (units/25 min)</p> <p>Time (min)</p> <p>Cold stress</p> <p>Antigen challenge</p> <p>Santos J et al. <i>Gastroenterology</i> 1998; 640:648</p> <p>B160</p>
<p>B161</p>	<p>Psychological Stress Converts Absorption of Water, Sodium, and Chloride to Secretion</p>	<p>Psychological Stress Converts Absorption of Water, Sodium, and Chloride to Secretion</p> <p>Water absorption (50 min)</p> <p>Electrolyte absorption (50 min)</p> <p>Control Stress Recovery</p> <p>Sodium Chloride</p> <p>Decreased absorption reflects increased secretion</p> <p>Barclay GR, Turnberg LA. <i>Gastroenterology</i> 1987; 93:91</p> <p>B161</p>

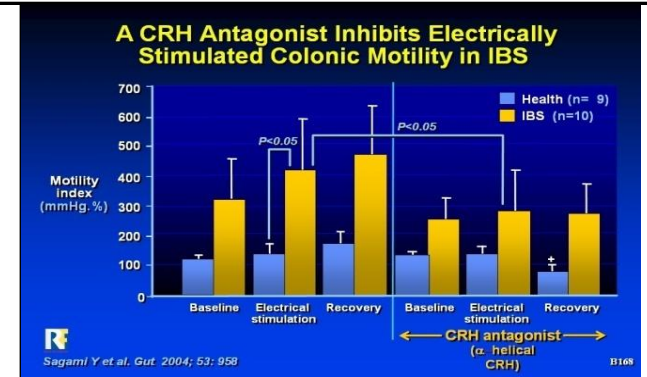
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<p>B162</p>	<p>Neonatal Stress Leads to Visceral Hypersensitivity and Altered Bowel Function in Adult Rats</p>	<p>Neonatal Stress Leads to Visceral Hypersensitivity and Altered Bowel Function in Adult Rats</p> <p>Colon irritation Colorectal distension or maternal separation</p> <p>Hypersensitivity without inflammation, constipation, diarrhea neuronal sensitization</p> <p>Week: 5, 6, 7</p> <p>Month 3</p> <p>Birth, 22 days, Resting Period, Testing Period</p> <p><i>Al-Chaer ED et al. Gastroenterology 2000; 119:1276</i> <i>Coutinho S et al. Am J Physiol 2002; 282: G307-G316</i></p> <p>B162</p>
<p>B163</p>	<p>Acute Psychological Stress Provokes Rectal Hypersensitivity to distension in IBS</p>	<p>Acute Psychological Stress Provokes Rectal Hypersensitivity to Distension in IBS</p> <p>Defecatory urge in response to rectal distension</p> <p>Distension pressure (mmHg)</p> <p>Before stress, During stress, After stress</p> <p>Distension sequence</p> <p>Health, IBS</p> <p><i>Possnerud J et al. Gut 2004; 53:1102</i></p> <p>B163</p>
<p>B164</p>	<p>Experimentally-Induced Anxiety Impairs Gastric Accommodation to a Meal</p>	<p>Experimentally Induced Anxiety Impairs Gastric Accommodation to a Meal</p> <p>14 healthy subjects</p> <p>Gastric barostat study with neutral or anxious emotional state modulation for 10 min postmeal</p> <p>Normal postprandial volume increase was significantly less after anxiety</p> <p>Intragastric balloon volume (ml)</p> <p>Time (min)</p> <p>Meal</p> <p>Neutral, Anxiety</p> <p><i>Geeraerts B et al. Gastroenterology 2005; 129:1437</i></p> <p>B164</p>

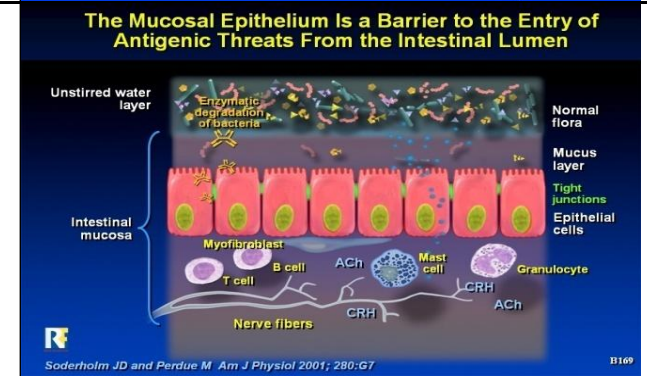
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<p>B165</p>	<p>Alteration of the MMC by Psychological Stress in Healthy Subjects and IBS Patients</p>	<p>Alteration of the MMC by Psychological Stress in Healthy Subjects and IBS Patients</p>  <table border="1"> <caption>Number of MMCs (per 8 hr)</caption> <thead> <tr> <th>State</th> <th>Health</th> <th>IBS</th> </tr> </thead> <tbody> <tr> <td>Asleep</td> <td>~7.5</td> <td>~6.5</td> </tr> <tr> <td>Awake</td> <td>~4.5</td> <td>~4.0</td> </tr> <tr> <td>Psychological stress</td> <td>~2.5</td> <td>~1.5</td> </tr> </tbody> </table> <p>McRae S et al. Gut 1982; 23:404</p>	State	Health	IBS	Asleep	~7.5	~6.5	Awake	~4.5	~4.0	Psychological stress	~2.5	~1.5												
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<p>B166</p>	<p>Functional GI Disorders: Delayed Gut Transit Is Associated With Female Gender and Depression</p>	<p>Functional GI Disorders: Delayed Gut Transit Is Associated With Female Gender and Depression</p> <p>110 FGID patients Gastric, small bowel, and colon scintigraphic transit assessed</p>  <table border="1"> <thead> <tr> <th></th> <th>Normal transit in all 3 regions</th> <th>Delayed transit in 1 region</th> <th>Delayed transit in 2 or 3 regions</th> </tr> </thead> <tbody> <tr> <td>F:M ratio</td> <td>2:1</td> <td>7:1*</td> <td>10:1*</td> </tr> <tr> <td>Depression score</td> <td>13(2.6)</td> <td>11 (1.2)</td> <td>16(3.2)*</td> </tr> <tr> <td>Hypochondriasis score</td> <td>2.6 (0.5)</td> <td>1.4 (0.2)*</td> <td>1.4 (0.2)*</td> </tr> </tbody> </table> <p>*P<0.05 vs normal transit</p> <p>Bennett EJ et al. Gut 2000; 46:83</p>		Normal transit in all 3 regions	Delayed transit in 1 region	Delayed transit in 2 or 3 regions	F:M ratio	2:1	7:1*	10:1*	Depression score	13(2.6)	11 (1.2)	16(3.2)*	Hypochondriasis score	2.6 (0.5)	1.4 (0.2)*	1.4 (0.2)*								
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Depression score	13(2.6)	11 (1.2)	16(3.2)*																							
Hypochondriasis score	2.6 (0.5)	1.4 (0.2)*	1.4 (0.2)*																							
<p>B167</p>	<p>Corticotropin-Releasing Factor (CRF) Provokes an Exaggerated Descending Colon Motor Response in IBS</p>	<p>Corticotropin-Releasing Factor (CRF) Provokes an Exaggerated Descending Colon Motor Response in IBS</p>  <table border="1"> <caption>Motility Index (mmHg %)</caption> <thead> <tr> <th>Time (min)</th> <th>Health</th> <th>IBS</th> </tr> </thead> <tbody> <tr> <td>-30</td> <td>~100</td> <td>~100</td> </tr> <tr> <td>-15</td> <td>~100</td> <td>~100</td> </tr> <tr> <td>0</td> <td>~300</td> <td>~650</td> </tr> <tr> <td>15</td> <td>~250</td> <td>~750</td> </tr> <tr> <td>30</td> <td>~150</td> <td>~750</td> </tr> <tr> <td>45</td> <td>~100</td> <td>~400*</td> </tr> <tr> <td>60</td> <td>~200</td> <td>~500*</td> </tr> </tbody> </table> <p>P<0.05 *</p> <p>Fukudo S et al. Gut 1998; 2:845-849</p>	Time (min)	Health	IBS	-30	~100	~100	-15	~100	~100	0	~300	~650	15	~250	~750	30	~150	~750	45	~100	~400*	60	~200	~500*
Time (min)	Health	IBS																								
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0	~300	~650																								
15	~250	~750																								
30	~150	~750																								
45	~100	~400*																								
60	~200	~500*																								

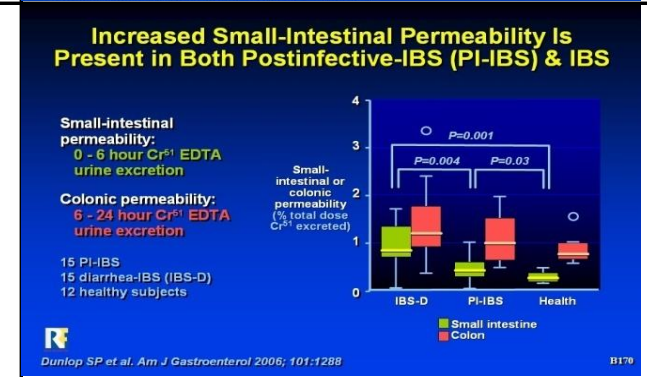
B168 A CRH Antagonist Inhibits Electrically-Stimulated Colonic Motility in IBS



B169 The Mucosal Epithelium Is a Barrier to the Entry of Antigenic Threats From the Intestinal Lumen



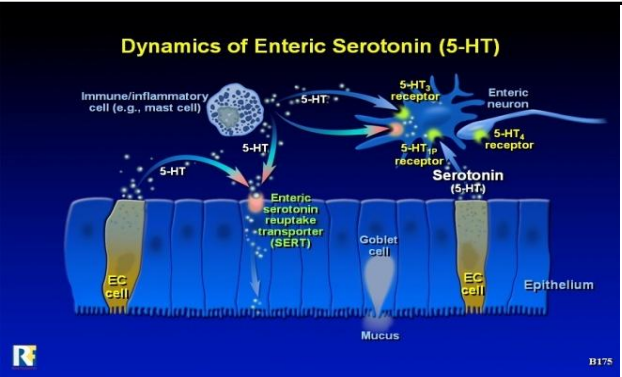
B170 Increased Small-Intestinal Permeability Is Present in Both Postinfective-IBS (PI-IBS) and IBS



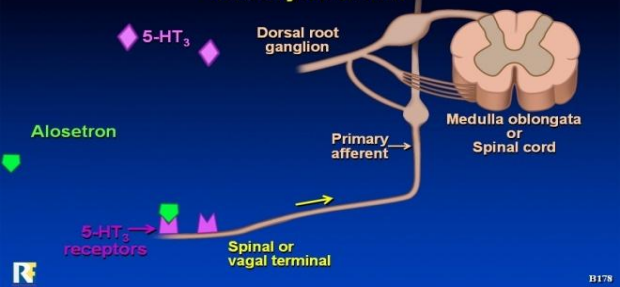
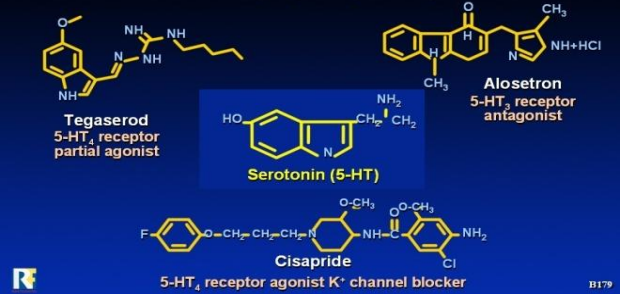
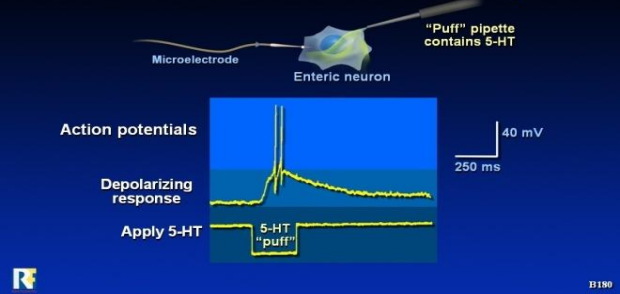
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<p>B171</p>	<p>Cold-Restraint Stress Increases Mucosal Permeability and Stimulates Secretion in Rats</p>	<p>Cold-Restraint Stress Increases Mucosal Permeability and Stimulates Secretion in Rats</p> <p>The first graph shows mucosal permeability (pmol/cm²/hr) for Control (~6), Cold-restraint stress (~18*), and CRF antagonist (~6**). The second graph shows mucosal secretion (μA/cm²) for Control (~60), Cold-restraint stress (~95*), and CRF antagonist (~60**). Significance markers: * P<0,05, ** P<0,01.</p> <p>Adapted from Saunders PR et al. Dig Dis Sci 2002; 47:208</p> <p>B171</p>
<p>B172</p>	<p>Stress in Mice Is Associated With Mast-Cell Hyperplasia and Increased Colonic Permeability</p>	<p>Stress in Mice Is Associated With Mast-Cell Hyperplasia and Increased Colonic Permeability</p> <p>The diagram shows mice with mast cell containing and mast cell deficient genotypes undergoing water-avoidance stress (1 hour/day x 5 days). The first bar graph shows mast cells (no./mm²) for Sham stress (~50) and Water stress (~400) in MC-containing mice. The second bar graph shows colonic permeability for Sham stress (~5) and Water stress (~25) in MC-containing mice, and Sham stress (~5) and Water stress (~5) in MC-deficient mice. Significance markers: ** P<0,01 vs all other groups.</p> <p>Adapted from Santos J et al. Gut 2001; 48:630</p> <p>B172</p>
<p>B173</p>	<p>Corticotropin-Releasing Hormone (CRH) Regulates In Vitro Permeability of Human Colonic Mucosa via Mast Cells</p>	<p>Corticotropin-Releasing Hormone (CRH) Regulates In Vitro Permeability of Human Colonic Mucosa via Mast Cells</p> <p>The graph shows mucosal permeability (Flux HRP in pmol/cm²/h) for 39 healthy subjects under three pretreatment conditions: None, CRH antagonist, and Mast-cell stabilizer. For each condition, Vehicle (blue) and CRH (yellow) are compared. Significance markers: P<0,05 for CRH vs Vehicle in the None and CRH antagonist groups.</p> <p>Colonic biopsies from 39 healthy subjects</p> <ul style="list-style-type: none"> Mucosal permeability (horseradish peroxidase, HRP) increased by CRH Increased permeability abolished by <ul style="list-style-type: none"> - CRH antagonist - Mast-cell stabilizer <p>Wallon C et al. Gut 2008; 57:50</p> <p>B173</p>
<p>B174</p>	<p>Section Title: Neuropharmacology of the Digestive Tract</p>	

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<p>B175</p>	<p>Dynamics of Enteric Serotonin (5-HT)</p>	 <p>Dynamics of Enteric Serotonin (5-HT)</p> <p>The diagram illustrates the production and signaling of 5-HT in the gut. An immune/inflammatory cell (e.g., mast cell) releases 5-HT, which binds to 5-HT₂ receptors on an enteric neuron. Additionally, an EC cell (enterochromaffin cell) produces 5-HT, which is transported by the enteric serotonin reuptake transporter (SERT) into the epithelium. In the epithelium, 5-HT can be released from EC cells and bind to 5-HT₁ receptors on enteric neurons. Goblet cells in the epithelium produce mucus. The diagram also shows 5-HT binding to 5-HT₄ receptors on enteric neurons.</p> <p>R B175</p>
<p>B176</p>	<p>Multiple Serotonergic (5-HT) Receptor Subtypes Are Expressed in the Gut</p>	<p>Multiple Serotonergic (5-HT) Receptor Subtypes Are Expressed in the Gut</p> <p>Five different serotonin receptor types are present in the mammalian gut</p> <p>5-HT₁ 5-HT₂ 5-HT₃ 5-HT₄ 5-HT₇</p> <p>Two main drug classes that act on 5-HT receptors have been developed for therapeutic purposes</p> <ul style="list-style-type: none"> • 5-HT₃ antagonists (e.g., alosetron, cilansetron) • 5-HT₄ agonists (e.g., tegaserod) <p>R B176</p>
<p>B177</p>	<p>Cisapride and Tegaserod Act at Presynaptic 5-HT₄ Receptors to Enhance the Amplitude of EPSPs at Enteric Nicotinic Synapses</p>	<p>Cisapride and Tegaserod Act at Presynaptic 5-HT Receptors to Enhance the Amplitude of EPSPs at Enteric Nicotinic Synapses</p> <p>The diagram shows a presynaptic 5-HT receptor on an enteric neuron. Cisapride and tegaserod bind to these receptors, stimulating acetylcholine release. This leads to stimulation of nicotinic receptors on the postsynaptic neuron, resulting in EPSPs (Excitatory postsynaptic potentials). A graph shows that the presence of cisapride or tegaserod increases the amplitude of the EPSPs compared to a control.</p> <p>R B177</p>

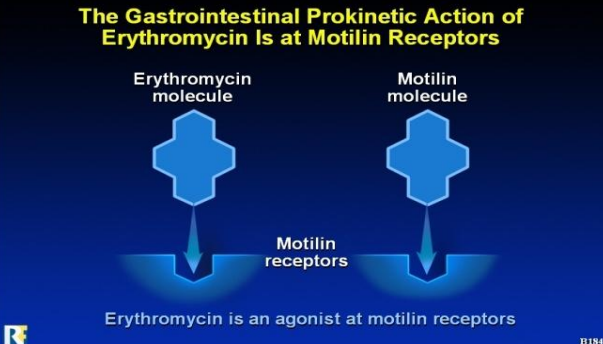
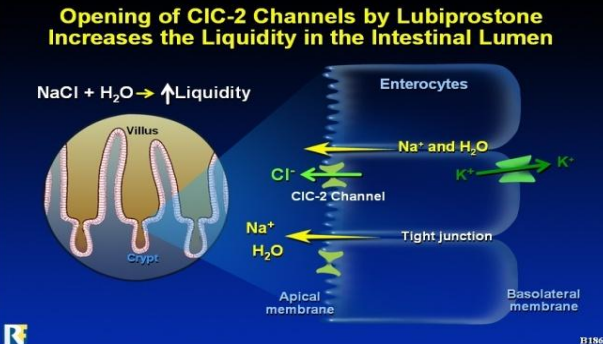
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<p>B178</p>	<p>Alosetron is an Antagonist at Serotonergic 5-HT₃ Receptors on Terminals of Spinal and Vagal Sensory Afferents</p>	<p>Alosetron Is an Antagonist at Serotonergic 5-HT₃ Receptors on Terminals of Spinal and Vagal Sensory Afferents</p>  <p>R B178</p>
<p>B179</p>	<p>Drugs Acting at Enteric Serotonergic (5-HT) Receptors</p>	<p>Drugs Acting at Enteric Serotonergic (5-HT) Receptors</p>  <p>R B179</p>
<p>B180</p>	<p>Serotonin (5-HT) Acts at 5-HT₃ Receptors to Excite Neurons in the Enteric Nervous System</p>	<p>Serotonin (5-HT) Acts at 5-HT Receptors to Excite Neurons in the Enteric Nervous System</p>  <p>R B180</p>

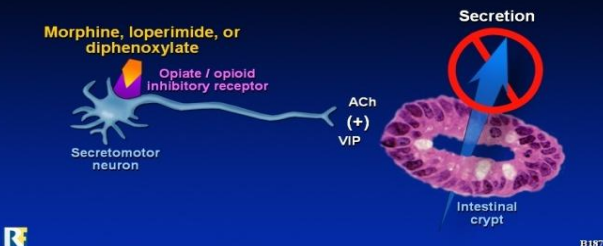
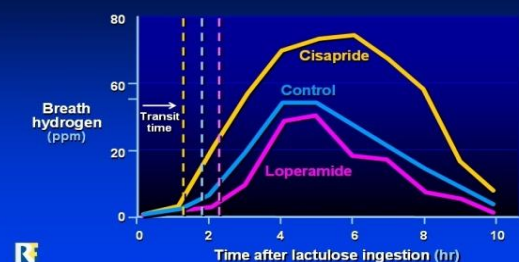
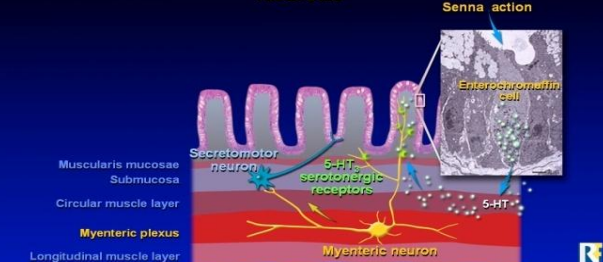
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<p>B181</p>	<p>Alosetron Blocks Serotonin-Evoked Excitation of Secretomotor Neurons</p>	<p>Alosetron Blocks Serotonin-Evoked Excitation of Secretomotor Neurons</p> <p>Alosetron 5-HT₃ antagonist</p> <p>5-HT₃</p> <p>Secretomotor neuron</p> <p>Serotonin 5-HT₃ excitatory receptor</p> <p>ACh (+) VIP</p> <p>Intestinal crypt</p> <p>Secretion</p> <p>R</p> <p>B181</p>
<p>B182</p>	<p>Domperidone Suppresses Presynaptic Inhibitory Action of Dopamine at the D₂ Receptor Subtype</p>	<p>Domperidone Suppresses Presynaptic Inhibitory Action of Dopamine at the D₂ Receptor Subtype</p> <p>Dopaminergic nerve fibers</p> <p>Storage vesicles of dopamine</p> <p>Dopamine</p> <p>Domperidone</p> <p>Presynaptic dopamine D₂ receptors</p> <p>Suppress ACh release</p> <p>Enteric neuron</p> <p>R</p> <p>B182</p>
<p>B183</p>	<p>Erythromycin Enhances Gastric Emptying by Stimulating Antral and Pyloric Contractions</p>	<p>Erythromycin Enhances Gastric Emptying by Stimulating Antral and Pyloric Contractions</p> <p>Placebo</p> <p>Antrum</p> <p>Pylorus</p> <p>100 mm Hg 1 min.</p> <p>Erythromycin</p> <p>Antrum</p> <p>Pylorus</p> <p>R</p> <p>Sarna SK et al. Gastroenterology 1991; 101:1488</p> <p>B183</p>

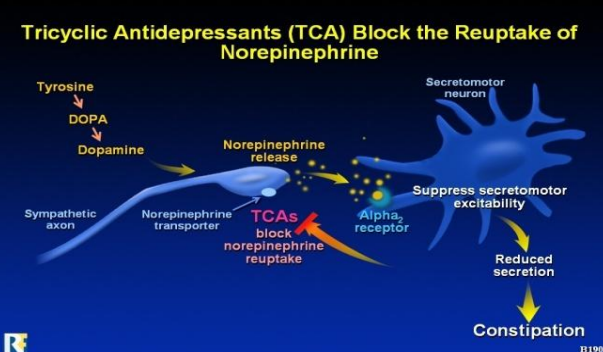
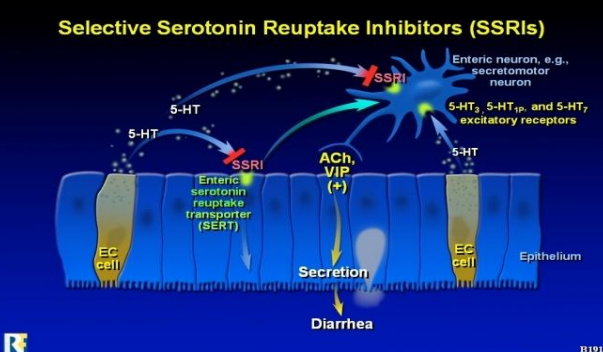
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<p>B184</p>	<p>The Gastrointestinal Prokinetic Action of Erythromycin Is at Motilin Receptors</p>	<p>The Gastrointestinal Prokinetic Action of Erythromycin Is at Motilin Receptors</p>  <p>Erythromycin is an agonist at motilin receptors</p> <p><small>B184</small></p>																					
<p>B185</p>	<p>Prokinetic Drugs Used to Enhance Gastric Emptying Have Different Sites and Mechanisms of Action</p>	<p>Prokinetic Drugs Used to Enhance Gastric Emptying Have Different Sites and Mechanisms of Action</p> <table border="1"> <thead> <tr> <th>Drug</th> <th>Mechanism of action</th> <th>Site</th> </tr> </thead> <tbody> <tr> <td>Metoclopramide</td> <td>Dopamine receptor antagonist stimulates acetylcholine release</td> <td>ENS</td> </tr> <tr> <td>Cisapride</td> <td>Stimulates acetylcholine release at enteric synapses and neuromuscular junctions. 5-HT₄ receptor partial agonist</td> <td>ENS</td> </tr> <tr> <td>Tegaserod</td> <td>Stimulates acetylcholine release at enteric synapses and neuromuscular junctions. 5-HT₄ receptor partial agonist</td> <td>ENS</td> </tr> <tr> <td>Erythromycin</td> <td>Motilin receptor agonist</td> <td>ENS smooth muscle</td> </tr> <tr> <td>Domperidone</td> <td>Dopamine D₂ receptor antagonist</td> <td>ENS</td> </tr> <tr> <td>Bethanechol</td> <td>Muscarinic receptor agonist</td> <td>ENS smooth muscle</td> </tr> </tbody> </table> <p><small>B185</small></p>	Drug	Mechanism of action	Site	Metoclopramide	Dopamine receptor antagonist stimulates acetylcholine release	ENS	Cisapride	Stimulates acetylcholine release at enteric synapses and neuromuscular junctions. 5-HT ₄ receptor partial agonist	ENS	Tegaserod	Stimulates acetylcholine release at enteric synapses and neuromuscular junctions. 5-HT ₄ receptor partial agonist	ENS	Erythromycin	Motilin receptor agonist	ENS smooth muscle	Domperidone	Dopamine D ₂ receptor antagonist	ENS	Bethanechol	Muscarinic receptor agonist	ENS smooth muscle
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<p>B186</p>	<p>Opening of ClC-2 Channels by Lubiprostone Increases the Liquidity in the Intestinal Lumen</p>	<p>Opening of ClC-2 Channels by Lubiprostone Increases the Liquidity in the Intestinal Lumen</p>  <p>$\text{NaCl} + \text{H}_2\text{O} \rightarrow \uparrow \text{Liquidity}$</p> <p>Enterocytes</p> <p>Cl⁻ ← ClC-2 Channel</p> <p>Na⁺ and H₂O →</p> <p>K⁺ →</p> <p>Tight junction</p> <p>Apical membrane</p> <p>Basolateral membrane</p> <p><small>B186</small></p>																					



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<p>B187</p>	<p>Opiates and Opioid Antidiarrheal Drugs Suppress Excitability of Secretomotor Neurons</p>	<p>Opiates and Opioid Antidiarrheal Drugs Suppress Excitability of Secretomotor Neurons</p>  <p>Morphine, loperimide, or diphenoxylate</p> <p>Opiate / opioid inhibitory receptor</p> <p>Secretomotor neuron</p> <p>ACh (+) VIP</p> <p>Secretion</p> <p>Intestinal crypt</p> <p>R</p> <p>B187</p>
<p>B188</p>	<p>Mouth to Cecum Transit Time Can Be Pharmacologically Regulated in Healthy Subjects</p>	<p>Mouth to Cecum Transit Time Can Be Pharmacologically Regulated in Healthy Subjects</p>  <p>Breath hydrogen (ppm)</p> <p>Transit time</p> <p>Cisapride</p> <p>Control</p> <p>Loperamide</p> <p>Time after lactulose ingestion (hr)</p> <p>R</p> <p>Oufir LE et al. Gut 1996; 38:870</p> <p>B188</p>
<p>B189</p>	<p>Stimulant Laxatives Evoke Release of Serotonin From Enterochromaffin Cells to Excite Secretomotor Neurons</p>	<p>Stimulant Laxatives Evoke Release of Serotonin From Enterochromaffin Cells to Excite Secretomotor Neurons</p>  <p>Senna action</p> <p>Enterochromaffin cell</p> <p>5-HT serotonergic receptors</p> <p>5-HT</p> <p>Myenteric neuron</p> <p>Secretomotor neuron</p> <p>Muscularis mucosae</p> <p>Submucosa</p> <p>Circular muscle layer</p> <p>Myenteric plexus</p> <p>Longitudinal muscle layer</p> <p>R</p> <p>B189</p>

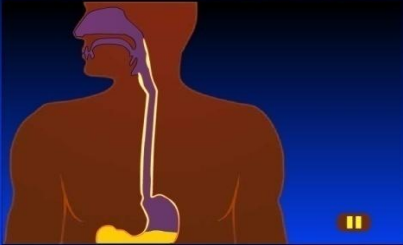
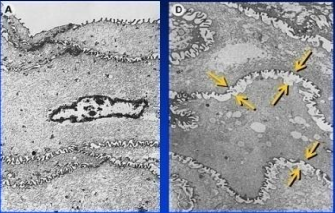
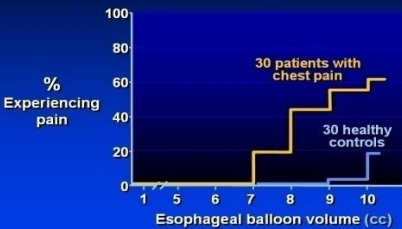
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B190	Tricyclic Antidepressants (TCA) Block the Reuptake of Norepinephrine	 <p>Tricyclic Antidepressants (TCA) Block the Reuptake of Norepinephrine</p> <p>The diagram illustrates the mechanism of TCA. It shows a sympathetic axon releasing norepinephrine into the synaptic cleft. The norepinephrine transporter (NET) is shown on the axon membrane, and TCA is shown blocking it. Norepinephrine release is also shown. The released norepinephrine binds to α_2 receptors on the secretomotor neuron, which suppresses its excitability and leads to reduced secretion. This results in constipation. The pathway starts with Tyrosine being converted to DOPA and then Dopamine. The sympathetic axon contains the norepinephrine transporter. The secretomotor neuron has α_2 receptors. The final outcome is constipation.</p> <p>R B190</p>
B191	Selective Serotonin Reuptake Inhibitors (SSRIs)	 <p>Selective Serotonin Reuptake Inhibitors (SSRIs)</p> <p>The diagram illustrates the mechanism of SSRIs. It shows an enteric neuron (e.g., secretomotor neuron) releasing 5-HT into the synaptic cleft. The enteric serotonin transporter (SERT) is shown on the neuron membrane, and SSRI is shown blocking it. 5-HT is also shown binding to $5-HT_2$, $5-HT_{10}$, and $5-HT_7$ excitatory receptors on the neuron. The neuron also releases ACh and VIP, which have a stimulatory effect (+) on the neuron. The neuron is shown secreting 5-HT, leading to diarrhea. The diagram also shows EC cells and epithelium. The final outcome is diarrhea.</p> <p>R B191</p>

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Diagnosis

Slide Number	Slide Title	Slide Image
D1	Functional Esophageal Disorders	<p>Functional Esophageal Disorders</p> <ul style="list-style-type: none"> • Functional heartburn • Functional chest pain of presumed esophageal origin • Functional dysphagia • Globus <p> D1</p>
D2	Functional Heartburn: Diagnostic Criteria	<p>Functional Heartburn: Diagnostic Criteria*</p> <ul style="list-style-type: none"> • Burning retrosternal discomfort or pain  • No evidence that acid reflux is the cause • No histopathology-based esophageal motility disorder  <p><small>*Criteria fulfilled for last 3 months Symptom onset at least 6 months prior to diagnosis</small></p> <p> D2</p> <p><small>Galmiche JP et al. Gastroenterology. 2006; 130: 1459</small></p>
D3	Functional Chest Pain of Presumed Esophageal Origin: Diagnostic Criteria	<p>Functional Chest Pain of Presumed Esophageal Origin: Diagnostic Criteria*</p> <ul style="list-style-type: none"> • Midline chest pain or discomfort that is not of burning quality  • No evidence that reflux is the cause • No histopathology-based esophageal motility disorder  <p><small>*Criteria fulfilled for last 3 months Symptom onset at least 6 months prior to diagnosis</small></p> <p> D3</p> <p><small>Galmiche JP et al. Gastroenterology. 2006; 130: 1459</small></p>

Computer-Based Learning Program
Diagnosis

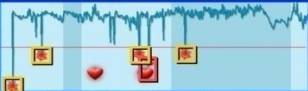

<p>D4</p>	<p>Proposed Mechanisms for Chest Pain of Presumed Esophageal Origin</p>	<p>Diagnosis</p> <p>Proposed Mechanisms for Chest Pain of Presumed Esophageal Origin</p>  <p>R</p> <p>D4</p>																								
<p>D5</p>	<p>Intercellular Spaces in Esophageal Squamous Epithelium by Transmission Electron Microscopy</p>	<p>Diagnosis</p> <p>Intercellular Spaces in Esophageal Squamous Epithelium by Transmission Electron Microscopy</p>  <p>Dilated intercellular spaces indicate increased mucosal permeability</p> <p>Acid has access to nerve endings in the epithelium</p> <p>Healthy Subject Patient with NERD</p> <p><i>Tobey NA et al. Gastroenterology, 1996; 111:1200</i></p> <p>R</p> <p>D5</p>																								
<p>D6</p>	<p>Hypersensitivity to Esophageal Balloon Distention in Patients with Unexplained Chest Pain</p>	<p>Diagnosis</p> <p>Hypersensitivity to Esophageal Balloon Distention in Patients with Unexplained Chest Pain</p>  <table border="1"> <caption>Data from Graph: Hypersensitivity to Esophageal Balloon Distention</caption> <thead> <tr> <th>Esophageal balloon volume (cc)</th> <th>% Experiencing pain (30 patients with chest pain)</th> <th>% Experiencing pain (30 healthy controls)</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>0</td> <td>0</td> </tr> <tr> <td>5</td> <td>0</td> <td>0</td> </tr> <tr> <td>6</td> <td>0</td> <td>0</td> </tr> <tr> <td>7</td> <td>20</td> <td>0</td> </tr> <tr> <td>8</td> <td>45</td> <td>0</td> </tr> <tr> <td>9</td> <td>60</td> <td>0</td> </tr> <tr> <td>10</td> <td>60</td> <td>10</td> </tr> </tbody> </table> <p>R</p> <p><i>Richter JE et al. Gastroenterology 1986; 91:845</i></p> <p>D6</p>	Esophageal balloon volume (cc)	% Experiencing pain (30 patients with chest pain)	% Experiencing pain (30 healthy controls)	1	0	0	5	0	0	6	0	0	7	20	0	8	45	0	9	60	0	10	60	10
Esophageal balloon volume (cc)	% Experiencing pain (30 patients with chest pain)	% Experiencing pain (30 healthy controls)																								
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Computer-Based Learning Program
Diagnosis




<p>D7</p>	<p>PPI Test for Unexplained Chest Pain</p>	<p>Diagnosis</p> <p>PPI Test for Unexplained Chest Pain</p> <p>37 patients with NCCP</p> <p>Endoscopy, 24-hr pH monitoring (23 GERD+, 14 GERD-)</p> <p>Omeprazole (40mg AM, 20mg PM) 1 week Placebo</p> <p>Crossover</p> <p>Positive PPI test: Pain >50% improved during PPI treatment</p> <p><small>Fass R et al. Gastroenterology 1998; 115:42</small></p>
<p>D8</p>	<p>Correlation of Chest Pain with Episodes of Acid Reflux</p>	<p>Correlation of Chest Pain with Episodes of Acid Reflux</p> <p>Esophageal pH</p> <p>Acid Reflux Episodes</p> <p>Chest Pain Episodes</p> <p>8AM Noon 4PM 8PM Midnight 8AM</p> <p><small>D8</small></p>
<p>D9</p>	<p>Combined Multichannel Intraluminal Impedance (MII) and pH Monitoring</p>	<p>Diagnosis</p> <p>Combined Multichannel Intraluminal Impedance (MII) and pH Monitoring</p> <p>MII</p> <p>Detects reflux of acidic and nonacidic material</p> <p>pH Sensors</p> <p>Lower esophageal sphincter (LES)</p> <p><small>Sifrim D et al. Gut. 2004; 53:1024</small></p> <p><small>D9</small></p>

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Diagnosis

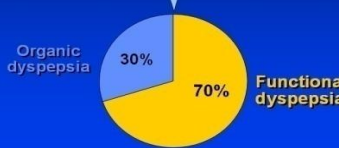

<p>D10</p>	<p>Combined MII and pH Monitoring</p>	<p>Diagnosis</p> <p>Combined MII and pH Monitoring</p>																																		
<p>D11</p>	<p>Possible Symptom-Reflux Correlations-Slide 1 of 4</p>	<p>Possible Symptom-Reflux Correlations</p> <table border="1"> <tr> <td colspan="2"></td> <td colspan="2">Symptoms</td> <td></td> </tr> <tr> <td colspan="2"></td> <td>+</td> <td>-</td> <td></td> </tr> <tr> <td rowspan="2">Reflux</td> <td>+</td> <td>S+R+</td> <td>S-R+</td> <td>R+ Total</td> </tr> <tr> <td>-</td> <td>S+R-</td> <td>S-R-</td> <td>R- Total</td> </tr> <tr> <td colspan="2"></td> <td>S+ Total</td> <td>S- Total</td> <td></td> </tr> </table> <p>R D11</p>			Symptoms					+	-		Reflux	+	S+R+	S-R+	R+ Total	-	S+R-	S-R-	R- Total			S+ Total	S- Total											
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		S+ Total	S- Total																																	
<p>D12</p>	<p>Symptom Index-Slide 2 of 4</p>	<p>Symptom Index</p> <table border="1"> <tr> <td colspan="2"></td> <td colspan="2">Symptoms</td> <td></td> </tr> <tr> <td colspan="2"></td> <td>+</td> <td>-</td> <td></td> </tr> <tr> <td rowspan="2">Reflux</td> <td>+</td> <td>1 S+R+</td> <td>S-R+</td> <td>R+ Total</td> </tr> <tr> <td>-</td> <td>1 S+R-</td> <td>S-R-</td> <td>R- Total</td> </tr> <tr> <td colspan="2"></td> <td>2 S+ Total</td> <td>S- Total</td> <td></td> </tr> <tr> <td colspan="2"></td> <td>Symptom Index</td> <td>S+R+</td> <td></td> </tr> <tr> <td colspan="2"></td> <td></td> <td>S+ Total</td> <td></td> </tr> </table> <p>R D12</p> <p>SI = $\frac{1}{2} = 50\%$ Positive SI $\geq 50\%$</p>			Symptoms					+	-		Reflux	+	1 S+R+	S-R+	R+ Total	-	1 S+R-	S-R-	R- Total			2 S+ Total	S- Total				Symptom Index	S+R+					S+ Total	
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<p>D13</p>	<p>Symptom Sensitivity Index-Slide 3 of 4</p>	<p>Symptom Sensitivity Index</p> <p>Symptoms + -</p> <table border="1"> <tr> <td></td> <td>S+R+ 1</td> <td>S-R+ 4</td> <td>R+ Total 5</td> </tr> <tr> <td>Reflux +</td> <td>S+R- 1</td> <td>S-R- 4</td> <td>R- Total 5</td> </tr> <tr> <td>Reflux -</td> <td>S+ Total 2</td> <td>S- Total 8</td> <td>R- Total 5</td> </tr> </table> <p>Symptom Sensitivity Index $\frac{S+R+}{R+ \text{ Total}}$ $SSI = \frac{1}{5} = 20\%$ Positive SSI $\geq 5\%$</p>  <p>R</p>		S+R+ 1	S-R+ 4	R+ Total 5	Reflux +	S+R- 1	S-R- 4	R- Total 5	Reflux -	S+ Total 2	S- Total 8	R- Total 5
	S+R+ 1	S-R+ 4	R+ Total 5											
Reflux +	S+R- 1	S-R- 4	R- Total 5											
Reflux -	S+ Total 2	S- Total 8	R- Total 5											
<p>D14</p>	<p>Symptom-Association Probability-Slide 4 of 4</p>	<p>Diagnosis</p> <p>Symptom-Association Probability (SAP)</p> <p>Divide 24 hours into 2-minute increments (720) and evaluate those increments for reflux and symptoms</p> <p>Symptoms + -</p> <table border="1"> <tr> <td></td> <td>3</td> <td>22</td> <td>25</td> </tr> <tr> <td>Reflux +</td> <td>1</td> <td>694</td> <td>695</td> </tr> <tr> <td>Reflux -</td> <td>4</td> <td>716</td> <td>720</td> </tr> </table> <p>Fisher Exact Test Probability that numbers in the contingency table are randomly distributed $P=0.0001$</p> <p>$SAP = (1.0 - P) \times 100\% = 99.99\%$ SAP >95% is significant</p> <p>R</p>		3	22	25	Reflux +	1	694	695	Reflux -	4	716	720
	3	22	25											
Reflux +	1	694	695											
Reflux -	4	716	720											
<p>D15</p>	<p>Functional Dysphagia: Diagnostic Criteria</p>	<p>Functional Dysphagia: Diagnostic Criteria*</p> <ul style="list-style-type: none"> • Sense of solid and/or liquid foods sticking, lodging, or passing abnormally through the esophagus • No evidence that reflux is the cause • No histopathology-based esophageal motility disorder <p>*Criteria fulfilled for last 3 months Symptom onset at least 6 months prior to diagnosis</p>  <p>R</p> <p><small>Galmiche JP et al. Gastroenterology. 2006; 130: 1459</small></p>												

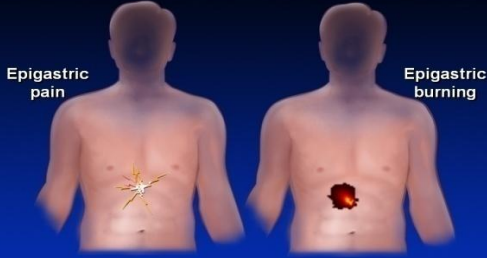
Computer-Based Learning Program
Diagnosis

<p>D16</p>	<p>Globus: Diagnostic Criteria</p>	<p>Globus: Diagnostic Criteria*</p> <ul style="list-style-type: none"> • Nonpainful sensation of a lump or foreign body in the throat • Occurrence of sensation between meals • No dysphagia or odynophagia • No evidence that reflux is the cause • No histopathology-based esophageal motility disorder <p>*Criteria fulfilled for last 3 months Symptom onset at least 6 months prior to diagnosis</p>  <p><small>Re Galimiche JP et al. Gastroenterology. 2006; 130: 1459. D16</small></p>
<p>D17</p>	<p>Functional Gastroduodenal Disorders</p>	<p>Functional Gastroduodenal Disorders</p> <ul style="list-style-type: none"> Functional dyspepsia Belching disorders Nausea and vomiting disorders Rumination syndrome in adults  <p><small>Re D17</small></p>
<p>D18</p>	<p>Functional Gastroduodenal Disorders: Functional Dyspepsia</p>	<p>Functional Gastroduodenal Disorders</p> <ul style="list-style-type: none"> Functional dyspepsia <ul style="list-style-type: none"> • Epigastric pain syndrome • Postprandial distress syndrome Belching disorders Nausea and vomiting disorders Rumination syndrome in adults  <p><small>Re D18</small></p>

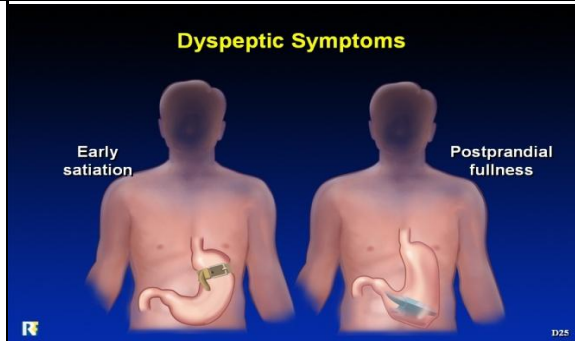

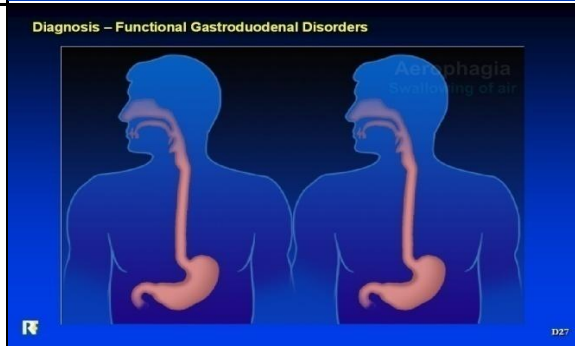
Computer-Based Learning Program
Diagnosis

D19	Uninvestigated Dyspepsia	<p>Uninvestigated Dyspepsia</p> <p>Symptoms that are considered to originate from the gastroduodenal region</p> <p>↓ Endoscopy . . .</p>  <p>Organic dyspepsia 30% Functional dyspepsia 70%</p> <p><small>© 2011 American College of Gastroenterology</small></p>
D20	Functional Dyspepsia: Two Categories	<p>Functional Dyspepsia</p> <p>Epigastric pain syndrome (EPS):</p> <p>Postprandial distress syndrome (PDS): meal-related FD</p>  <p>Epigastric pain Epigastric burning Early Satiation Postprandial heaviness or fullness</p> <p><small>© 2011 American College of Gastroenterology</small></p>
D21	Functional Dyspepsia: Diagnostic Criteria	<p>Functional Dyspepsia: Diagnostic Criteria*</p> <p>One or more of</p> <ul style="list-style-type: none">• Epigastric pain• Epigastric burning• Early satiation• Postprandial fullness <p>AND</p> <p>No evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms</p> <p><small>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</small></p> <p><small>© 2011 American College of Gastroenterology</small></p>

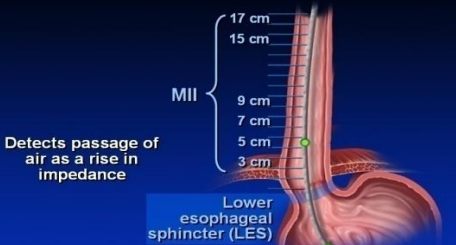
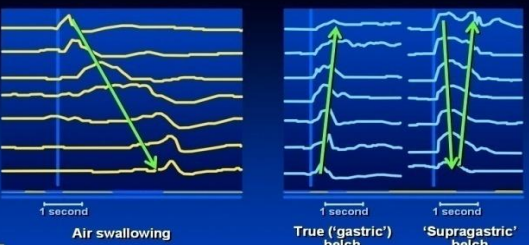
Computer-Based Learning Program
Diagnosis

<p>D22</p>	<p>Dyspeptic Symptoms</p>	<p>Dyspeptic Symptoms</p>  <p>Epigastric pain</p> <p>Epigastric burning</p> <p><small>R</small></p> <p><small>D22</small></p>
<p>D23</p>	<p>Epigastric Pain Syndrome: Diagnostic Criteria</p>	<p>Epigastric Pain Syndrome: Diagnostic Criteria*</p> <p>Must include ALL of the following:</p> <ol style="list-style-type: none"> 1. Pain or burning localized to the epigastrium, of at least moderate severity at least once per week 2. The pain is intermittent 3. Not generalized or localized to other abdominal or chest regions 4. Not relieved by defecation or passage of flatus 5. Not fulfilling criteria for biliary pain <p>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</p> <p><small>R</small></p> <p><small>Tack J et al. Gastroenterology, 2006; 130:1466</small></p> <p><small>D23</small></p>
<p>D24</p>	<p>Postprandial Distress Syndrome: Diagnostic Criteria</p>	<p>Postprandial Distress Syndrome: Diagnostic Criteria*</p> <p>Bothersome postprandial fullness, after ordinary-sized meals, at least several times per week,</p> <p>OR</p> <p>Early satiation that prevents finishing a regular meal, at least several times per week</p> <p>AND</p> <p>No evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms</p> <p>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</p> <p><small>R</small></p> <p><small>Tack J et al. Gastroenterology, 2006; 130:1466.</small></p> <p><small>D24</small></p>




Computer-Based Learning Program
Diagnosis

D25	Dyspeptic Symptoms	
D26	Functional Gastroduodenal Disorders: Belching Disorders	
D27	Aerophagia	

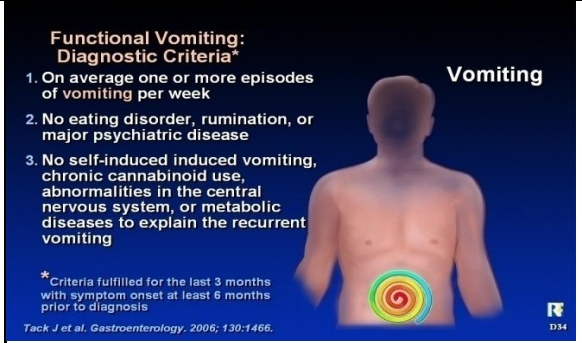
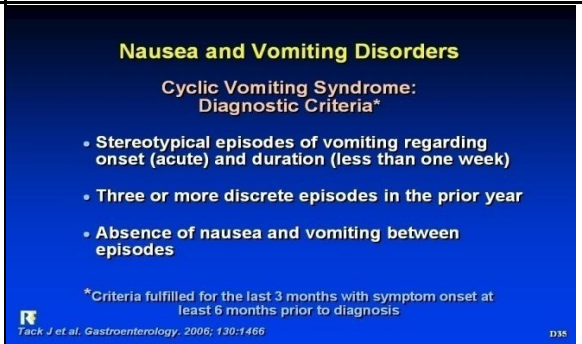
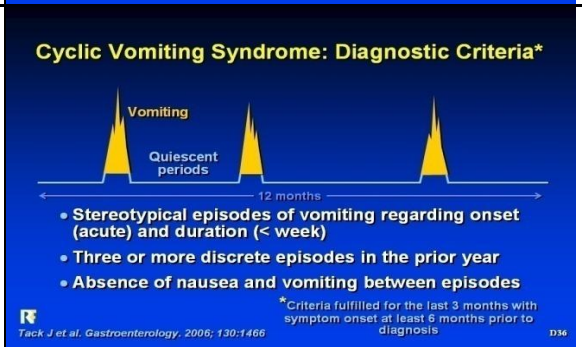
Computer-Based Learning Program
Diagnosis

<p>D28</p>	<p>Belching Disorders: Diagnostic Criteria</p>	<p>Belching Disorders: Diagnostic Criteria*</p> <p>Aerophagia:</p> <ul style="list-style-type: none"> • Troublesome repetitive belching at least several times a week, and • Air swallowing that is objectively observed or measured <p>Unspecified excessive belching:</p> <ul style="list-style-type: none"> • Troublesome repetitive belching at least several times a week, and • No evidence that excessive air swallowing underlies the symptom <p>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</p> <p><small>Tack J et al. Gastroenterology. 2006; 130:1466</small></p> <p><small>D28</small></p>
<p>D29</p>	<p>Multichannel Intraluminal Impedance (MII) Monitoring</p>	<p>Multichannel Intraluminal Impedance (MII) Monitoring</p>  <p>Detects passage of air as a rise in impedance</p> <p><small>D29</small></p>
<p>D30</p>	<p>MII Monitoring</p>	<p>MII Monitoring</p>  <p><small>D30</small></p>


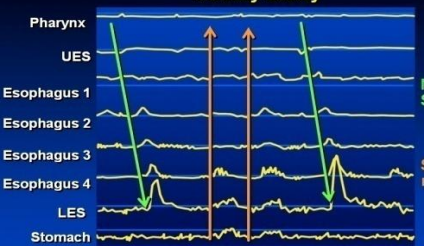
Computer-Based Learning Program
Diagnosis

D31	Functional Gastroduodenal Disorders: Nausea and Vomiting Disorders	<p>Functional Gastroduodenal Disorders</p> <p>Functional dyspepsia Belching disorders</p> <p>Nausea and vomiting disorders</p> <ul style="list-style-type: none">• Chronic idiopathic nausea• Functional vomiting• Cyclic vomiting syndrome <p>Rumination syndrome in adults</p>  <p><small>D31</small></p>
D32	Nausea and Vomiting	<p>Diagnosis – Functional Gastroduodenal Disorders</p> <p>Nausea Queasiness or sick sensation; a feeling of the need to vomit</p> <p>Vomiting Forceful oral expulsion of gastric contents; usually preceded by retching</p>  <p><small>D32</small></p>
D33	Chronic Idiopathic Nausea: Diagnostic Criteria	<p>Nausea</p>  <p>Chronic Idiopathic Nausea: Diagnostic Criteria*</p> <ol style="list-style-type: none">1. Bothersome nausea, occurring at least several times per week2. Not usually associated with vomiting3. Absence of abnormalities at upper endoscopy or metabolic disease that explain the nausea <p>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</p> <p><small>Tack J et al. Gastroenterology, 2006; 130:1466. <small>D33</small></small></p>

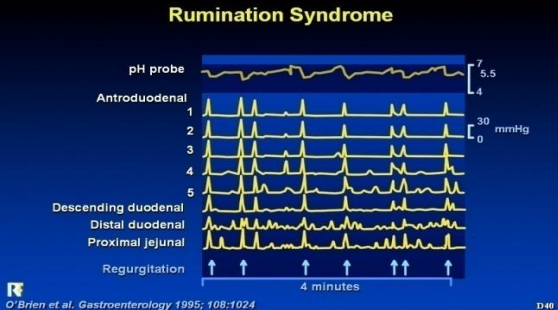


Computer-Based Learning Program
Diagnosis

<p>D34</p>	<p>Functional Vomiting: Diagnostic Criteria</p>	<p>Functional Vomiting: Diagnostic Criteria*</p> <ol style="list-style-type: none"> 1. On average one or more episodes of vomiting per week 2. No eating disorder, rumination, or major psychiatric disease 3. No self-induced induced vomiting, chronic cannabinoid use, abnormalities in the central nervous system, or metabolic diseases to explain the recurrent vomiting <p>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</p> <p>Tack J et al. <i>Gastroenterology</i>, 2006; 130:1466.</p> 
<p>D35</p>	<p>Cyclic Vomiting Syndrome: Diagnostic Criteria-Slide 1 of 2</p>	<p>Nausea and Vomiting Disorders</p> <p>Cyclic Vomiting Syndrome: Diagnostic Criteria*</p> <ul style="list-style-type: none"> • Stereotypical episodes of vomiting regarding onset (acute) and duration (less than one week) • Three or more discrete episodes in the prior year • Absence of nausea and vomiting between episodes <p>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</p> <p>Tack J et al. <i>Gastroenterology</i>, 2006; 130:1466</p> 
<p>D36</p>	<p>Cyclic Vomiting Syndrome: Diagnostic Criteria-Slide 2 of 2</p>	<p>Cyclic Vomiting Syndrome: Diagnostic Criteria*</p>  <ul style="list-style-type: none"> • Stereotypical episodes of vomiting regarding onset (acute) and duration (< week) • Three or more discrete episodes in the prior year • Absence of nausea and vomiting between episodes <p>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</p> <p>Tack J et al. <i>Gastroenterology</i>, 2006; 130:1466</p>





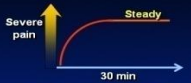


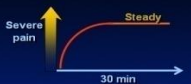

Computer-Based Learning Program
Diagnosis

<p>D37</p>	<p>Functional Gastroduodenal Disorders: Rumination Syndrome</p>	<p>Functional Gastroduodenal Disorders</p> <ul style="list-style-type: none"> Functional dyspepsia Belching disorders Nausea and vomiting disorders Rumination syndrome in adults  <p><small>D37</small></p>
<p>D38</p>	<p>Rumination Syndrome: Diagnostic Criteria</p>	<p>Rumination Syndrome: Diagnostic Criteria*</p> <p>Must include BOTH of the following:</p> <ul style="list-style-type: none"> Persistent or recurrent regurgitation of recently ingested food into the mouth with subsequent spitting or remastication and swallowing Regurgitation is not preceded by retching <p>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</p> <p>Supportive criteria:</p> <ul style="list-style-type: none"> Regurgitation events are usually not preceded by nausea Cessation of the process when the regurgitated material becomes acidic Regurgitant contains recognizable food with a pleasant taste <p><small>Tack J et al. Gastroenterology, 2006; 130:1466.</small></p> <p><small>D38</small></p>
<p>D39</p>	<p>Esophagogastric Manometry in the Rumination Syndrome</p>	<p>Rumination Syndrome Motility Study</p>  <p><small>D39</small></p>

Computer-Based Learning Program
Diagnosis

D40	Antroduodenal Manometry and pH Monitoring of the Distal Esophagus in the Rumination Syndrome	 <p>Rumination Syndrome</p> <p>pH probe Antroduodenal 1 2 3 4 5 Descending duodenal Distal duodenal Proximal jejunal Regurgitation</p> <p>4 minutes</p> <p><small>O'Brien et al. Gastroenterology 1995; 108:1024</small></p> <p>D40</p>
D41	Functional Biliary Disorders	 <p>Functional Biliary Disorders Encompass Motility Abnormalities of the Gallbladder and the Sphincter of Oddi and Include . . .</p> <ul style="list-style-type: none">• Functional gallbladder disorder• Functional biliary sphincter of Oddi disorder <p><small>Behar J et al. Gastroenterology. 2006; 130:1498</small></p> <p>D41</p>
D42	Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria-Slide 1 of 5	 <p>Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria</p> <ul style="list-style-type: none">• Pain located in the epigastrium and/or right-upper quadrant <p><small>Behar J et al. Gastroenterology. 2006; 130:1498</small></p> <p>D42</p>


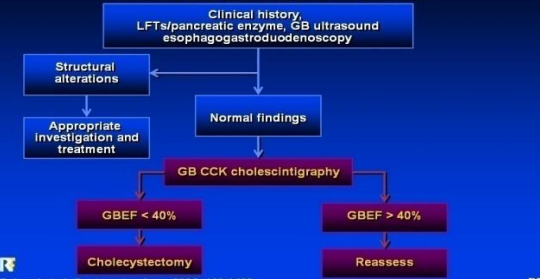
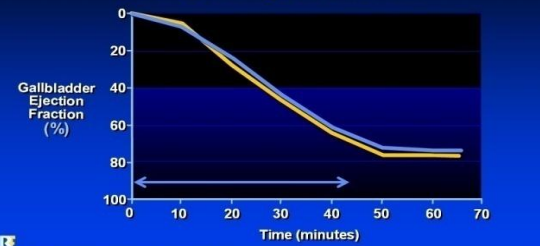
Computer-Based Learning Program
Diagnosis

D43	Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria-Slide 2 of 5	<p>Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria</p>  <ul style="list-style-type: none">• Pain located in the epigastrium and/or right-upper quadrant• Pain is severe enough to interrupt daily activities or require visit to ER  <p><small>Behar J et al. Gastroenterology, 2006; 130:1498</small></p> <p>D43</p>
D44	Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria-Slide 3 of 5	<p>Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria</p>  <ul style="list-style-type: none">• Pain located in the epigastrium and/or right upper quadrant• Pain is severe enough to interrupt daily activities or require visit to ER   <ul style="list-style-type: none">• Pain builds up to a steady level and lasts more than 30 minutes <p><small>Behar J et al. Gastroenterology, 2006; 130:1498</small></p> <p>D44</p>
D45	Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria-Slide 4 of 5	<p>Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria</p>  <ul style="list-style-type: none">• Pain located in the epigastrium and/or right-upper quadrant• Pain is severe enough to interrupt daily activities or require visit to ER   <ul style="list-style-type: none">• Episodes lasting 30 minutes and pain builds up to a steady level• Recurrent symptoms occurring at different intervals (not daily)  <p><small>Behar J et al. Gastroenterology, 2006; 130:1498</small></p> <p>D45</p>

Computer-Based Learning Program
Diagnosis

<p>D46</p>	<p>Rome III Diagnostic Criteria for Gallbladder and Sphincter of Oddi Pain-Slide 5 of 5</p>	<p>Gall Bladder and Sphincter of Oddi Pain</p>  <ul style="list-style-type: none"> • Pain located in the epigastrium and/or right upper quadrant • Pain is severe enough to interrupt daily activities or require visit to ER • Recurrent symptoms occurring at different intervals (not daily) • Episodes lasting 30 minutes and pain builds up to a steady level  <p>H HOSPITAL</p> <p><small>Behar J et al. Gastroenterology, 2006; 130:1498</small></p> <p>D46</p>
<p>D47</p>	<p>Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria</p>	<p>Gallbladder and Sphincter of Oddi Pain: Diagnostic Criteria (Continued)</p> <div style="display: flex; justify-content: space-between;"> <div style="border: 1px solid black; padding: 5px; width: 45%;"> <p>Not Relieved by</p> <ul style="list-style-type: none"> • Bowel Movements • Postural Change • Antacids </div> <div style="border: 1px solid black; padding: 5px; width: 45%;"> <p>Supportive Criteria</p> <p>Pain may present with one or more:</p> <ul style="list-style-type: none"> • Nausea and vomiting • Radiation to the back and/or right infra-subscapular region • Awakening from sleep at night </div> </div> <p><small>Behar J et al. Gastroenterology, 2006; 130:1498</small></p> <p>D47</p>
<p>D48</p>	<p>Functional Biliary Disorders: Clinical Presentation and Differential Diagnosis</p>	<p>Diagnose to Exclude Disorders</p>  <p><small>Behar J et al. Gastroenterology, 2006; 130:1498</small></p> <p>D48</p>

Computer-Based Learning Program
Diagnosis

<p>D49</p>	<p>Functional Biliary Disorders</p>	<p>Functional Biliary Disorders</p> <ul style="list-style-type: none"> • These are low-prevalence conditions with clinical presentation that is often similar to the following high-prevalence conditions:  <p>Main Goal Is To Avoid Doing Too Much</p> <p><small>D49</small></p>
<p>D50</p>	<p>Rome III Algorithm for Functional Gallbladder Disorder</p>	<p>Rome III Algorithm for Functional Gallbladder Disorder</p>  <p><small>Behar J et al. Gastroenterology. 2006; 130:1498</small></p> <p><small>D50</small></p>
<p>D51</p>	<p>Scintigraphic Gallbladder Ejection Fraction (GBEF) During CCK Infusion</p>	<p>Scintigraphic Gallbladder Ejection Fraction (GBEF) During CCK Infusion</p>  <p><small>Yap L. et al. Gastroenterology 1991; 101:786</small></p> <p><small>D51</small></p>

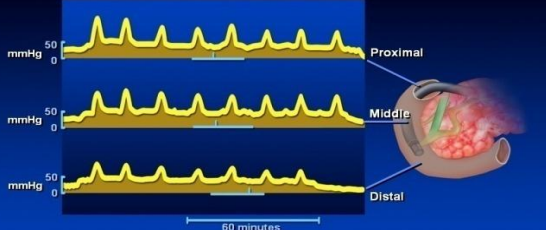

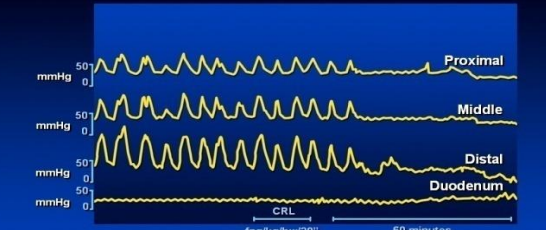
Computer-Based Learning Program
Diagnosis


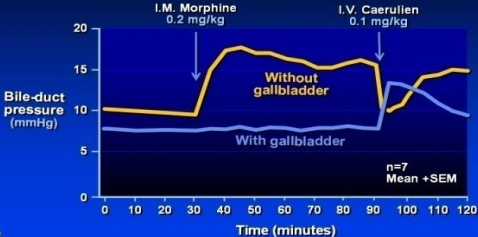
<p>D52</p>	<p>Pain Relief and Histological GB Findings After Cholecystectomy According to GBEF in GB Dysfunction</p>	<p>Pain Relief and Histological GB Findings After Cholecystectomy According to GBEF in GB Dysfunction</p> <table border="1"> <thead> <tr> <th rowspan="2"></th> <th colspan="2">% Pain Relief</th> <th colspan="2">% Abnormal GB Histology</th> </tr> <tr> <th>Yap</th> <th>Westlake</th> <th>Yap</th> <th>Westlake</th> </tr> </thead> <tbody> <tr> <td>GBEF < 40%</td> <td>90</td> <td>65</td> <td>92</td> <td>71</td> </tr> <tr> <td>GBEF ≥ 40%</td> <td>57</td> <td>100</td> <td>42</td> <td>68</td> </tr> </tbody> </table> <p><small>Yap L et al. Gastroenterology, 1991; 101:786 Westlake PJ et al. Am J Gastroenterol, 1990; 85:986</small></p>		% Pain Relief		% Abnormal GB Histology		Yap	Westlake	Yap	Westlake	GBEF < 40%	90	65	92	71	GBEF ≥ 40%	57	100	42	68
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<p>D53</p>	<p>Proposed Origin of Defective Gallbladder Emptying and Pain</p>	<p>Proposed Origin of Defective Gallbladder Emptying and Pain</p> <pre> graph TD Lithogenic[Lithogenic bile] --> Immune[Mucosal immune response] Idiopathic[Idiopathic] --> Immune Idiopathic --> Contractility[Defective gall bladder muscle contractility] Immune --> Inflammation[Mucosal inflammation] Inflammation --> Cholecystitis[Acute/chronic cholecystitis] Cholecystitis --> Pain[Biliary pain] Contractility --> Pain </pre> <p><small>RE</small></p>																			
<p>D54</p>	<p>Epidemiology of Functional Gallbladder Disorder</p>	<p>Epidemiology of Functional Gallbladder Disorder</p> <p>Prevalence of biliary-like pain in GB ultrasound-negative population</p> <table border="1"> <tbody> <tr> <td>Men^{1,2}</td> <td>7.6%</td> </tr> <tr> <td>Women^{1,2}</td> <td>20.7%</td> </tr> <tr> <td>Men and women³</td> <td>2.4%</td> </tr> </tbody> </table> <p><small>¹ GREPCO, Hepatology, 1988; 8:904 ² GREPCO, Am J Epidemiol, 1984; 119:796 ³ Barbara L et al. Hepatology, 1987; 7:913</small></p> <p><small>RE</small></p>	Men^{1,2}	7.6%	Women^{1,2}	20.7%	Men and women³	2.4%													
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Diagnosis

<p>D55</p>	<p>Rome III Algorithm for Functional Biliary Sphincter of Oddi Disorders</p>	<p>Rome III Algorithm for Functional Biliary Sphincter of Oddi Disorders</p> <p>Cholecystectomy, clinical history, LFTs/pancreatic enzyme, abdominal US esophagogastroduodenoscopy EUS, MRCP</p> <p>Structural alterations explain symptoms → Appropriate investigation and treatment</p> <p>Biliary type I → Milwaukee Classification Revised + Pain and + ↑LFTs in 2 occasions and + Dilated CBD >8mm</p> <p>Biliary type II → Pain and one type I criteria</p> <p>Biliary type III → Pain and no type I criteria</p> <p><small>Behar J et al. Gastroenterology, 2006; 130:1498 D55</small></p>
<p>D56</p>	<p>Rome III Algorithm for Functional Biliary Sphincter of Oddi Disorders</p>	<p>Rome III Algorithm for Functional Biliary Sphincter of Oddi Disorders</p> <p>Cholecystectomy, clinical history, LFTs/pancreatic enzyme, abdominal US esophagogastroduodenoscopy EUS, MRCP</p> <p>Structural alterations explain symptoms → Appropriate investigation and treatment</p> <p>Biliary type I → ES</p> <p>Biliary type II → ERCP with SOM</p> <p>Biliary type III → ERCP with SOM</p> <p>ERCP with SOM → Abnormal SOM → ES</p> <p>ERCP with SOM → Normal SOM → Reassess</p> <p><small>Behar J et al. Gastroenterology, 2006; 130:1498 D56</small></p>
<p>D57</p>	<p>Sphincter of Oddi (SO) Motor Abnormalities</p>	<p>Sphincter of Oddi Motor Abnormalities</p> <p>Sphincter of Oddi Stenosis</p> <ul style="list-style-type: none"> • Hypertonicity unaffected by muscle relaxants <p>Sphincter of Oddi Dyskinesia</p> <ul style="list-style-type: none"> • Hypertonicity affected by muscle relaxants • Paradoxical response to CCK • Tachyoddia • Increased retrograde contractions <p><small>D57</small></p>

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D58	Endoscopic Manometry of the Sphincter of Oddi in a Patient with Normal Motor Activity	<p>Endoscopic Manometry of the Sphincter of Oddi</p>  <p>mmHg 50 0 Proximal mmHg 50 0 Middle mmHg 50 0 Distal</p> <p>60 minutes</p> <p>Normal phase Pmax<40 mmHg</p> <p>D58</p>
D59	Endoscopic Manometry in a Patient with Sphincter of Oddi Hypertonicity	<p>Endoscopic Manometry Demonstrating Sphincter of Oddi Hypertonicity as Recorded by 3 Sensors</p>  <p>mmHg 50 0 Proximal mmHg 50 0 Middle mmHg 50 0 Distal</p> <p>60 minutes</p> <p>D59</p>
D60	Endoscopic Sphincter of Oddi Manometry in a Patient with Tachyoddia	<p>Endoscopic Manometry of the Sphincter of Oddi: Tachyoddia Blocked by CCK-Agonist Caerulein (CRL)</p>  <p>mmHg 50 0 Proximal mmHg 50 0 Middle mmHg 50 0 Distal mmHg 50 0 Duodenum</p> <p>60 minutes</p> <p>CRL</p> <p>D60</p>

<p>D61</p>	<p>Biliary (Choledocho) Scintigraphy</p>	<p>Biliary (Choledocho) Scintigraphy</p>  <table border="1"> <thead> <tr> <th>Case series</th> <th>vs Manometry</th> <th>vs Sphincterotomy</th> </tr> </thead> <tbody> <tr> <td>Without stimulus</td> <td>Sens (%)Spec (%)</td> <td>Sens (%)</td> </tr> <tr> <td>Corazzieri et al. ('91, '94, '02)</td> <td>83 100</td> <td>93</td> </tr> <tr> <td>Madacsy et al. 2000</td> <td>89 100</td> <td>NA</td> </tr> <tr> <td>With CCK stimulus</td> <td></td> <td></td> </tr> <tr> <td>Madacsy et al. 2000</td> <td>0 100</td> <td>NA</td> </tr> <tr> <td>Craig et al. 2003</td> <td>13 95</td> <td>NA</td> </tr> <tr> <td>Sostre et al. 1992</td> <td>100 100</td> <td>NA</td> </tr> </tbody> </table> <p><small>Corazzieri E et al. Gut. 2003; 52:1655</small></p>	Case series	vs Manometry	vs Sphincterotomy	Without stimulus	Sens (%)Spec (%)	Sens (%)	Corazzieri et al. ('91, '94, '02)	83 100	93	Madacsy et al. 2000	89 100	NA	With CCK stimulus			Madacsy et al. 2000	0 100	NA	Craig et al. 2003	13 95	NA	Sostre et al. 1992	100 100	NA
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<p>D62</p>	<p>Common Bile Duct (CBD) Pressure in the Absence or Presence of a Gallbladder</p>	<p>Common Bile Duct (CBD) Pressure in the Absence or Presence of a Gallbladder</p>  <p><small>Tanaka M et al. Gastroenterology, 1984; 87:1154</small></p>																								
<p>D63</p>	<p>Epidemiology of Functional Sphincter of Oddi Disorders</p>	<p>Epidemiology of Functional Sphincter of Oddi Disorders</p> <p>Postcholecystectomy patients</p> <ul style="list-style-type: none"> • Biliary pain in US negative population¹ <ul style="list-style-type: none"> US Householder Survey 1.5% • Manometric evidence of SO dysfunction² <ul style="list-style-type: none"> Consecutive series 0.8% Selected symptomatic patients 14.0% <p><small>1.Drossman DA et al. Dig Dis Sci 1993; 38:1569 2.Bar-Meir S et al. Hepatology, 1984; 4:328</small></p>																								

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D64	Functional Pancreatic Sphincter of Oddi Disorder: Diagnostic Criteria	<p>Functional Pancreatic Sphincter of Oddi Disorder: Diagnostic Criteria</p> <p>Must include both of the following:</p> <ol style="list-style-type: none">1. Criteria for functional gallbladder and sphincter of Oddi disorder2. Elevated amylase/lipase <p><small>Behar J et al. Gastroenterology, 2006; 130:1498 D64</small></p>
D65	Rome III Diagnostic and Therapeutical Algorithm for Functional Pancreatic SO Disorder	<p>Rome III Algorithm for Functional Pancreatic Sphincter of Oddi Disorder</p> <p>Clinical history of recurrent moderate-to-severe epigastric pain. Elevated amylase and lipase. No association with alcohol, gallstones, drugs</p> <p>↓</p> <p>Diagnostic ERCP</p> <p>↓</p> <p>Structural abnormalities → Sphincterotomy</p> <p>No structural abnormalities → SO manometry</p> <p>SO manometry</p> <p>↓</p> <p>Abnormal → Sphincterotomy</p> <p>Normal → Reassess</p> <p><small>Behar J et al. Gastroenterology, 2006; 130:1498 D65</small></p>
D66	Functional Bowel Disorders	<p>Functional Bowel Disorders</p> <ul style="list-style-type: none">• Irritable bowel syndrome• Functional bloating• Functional constipation• Functional diarrhea• Unspecified functional disorder <p><small>Behar J et al. Gastroenterology, 2006; 130:1498 D66</small></p>

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<p>D67</p>	<p>Irritable Bowel Syndrome: Diagnostic Criteria</p>	<p>Irritable Bowel Syndrome: Diagnostic Criteria*</p> <p>Recurrent abdominal pain or discomfort at least 3 days/month associated with two or more of the following:</p> <ul style="list-style-type: none"> • Improvement with defecation • Onset associated with a change in the frequency of stool • Onset associated with a change in the form of stool <p><small>*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</small></p> <p><small>R Longstreth GF et al. Gastroenterology. 2006; 130:1480 D67</small></p>		
<p>D68</p>	<p>History and Physical Examination for Lower GI Symptoms</p>	<p>History and Physical Examination for Lower GI Symptoms</p> <table border="0"> <tr> <td data-bbox="1375 657 1627 868"> <p>History</p> <ul style="list-style-type: none"> • Presenting symptoms • Establish history timeline • Presence of alarm signals • Family history: IBS, organic GI disorder • Diet • Review current medications </td> <td data-bbox="1648 657 1900 812"> <p>Examination</p> <ul style="list-style-type: none"> • Signs of systemic and local diseases that might cause constipation • Assess the anorectum and pelvic floor muscles • Other relevant abnormalities </td> </tr> </table> <p><small>R D68</small></p>	<p>History</p> <ul style="list-style-type: none"> • Presenting symptoms • Establish history timeline • Presence of alarm signals • Family history: IBS, organic GI disorder • Diet • Review current medications 	<p>Examination</p> <ul style="list-style-type: none"> • Signs of systemic and local diseases that might cause constipation • Assess the anorectum and pelvic floor muscles • Other relevant abnormalities
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<p>D69</p>	<p>Alarm Features for Organic Disorders</p>	<p>Alarm Features for Organic Disorders</p> <ul style="list-style-type: none"> • Age ≥50 years old • Blood in stools • Nocturnal symptoms • Weight loss (unintentional) • Change in symptoms • Recent antibiotics • Family history of organic GI disease <div data-bbox="1648 1023 1858 1169">  <p><small>If alarm features are present, investigate and treat appropriately</small></p> </div> <p><small>R D69</small></p>		

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<p>D70</p>	<p>Usefulness of Red Flags</p>	<p>Usefulness of Red Flags</p> <p>Review of >1400 charts Diagnoses: IBS, abdominal pain, diarrhea, constipation</p> <p>Average number of red flags present per patient:</p> <ul style="list-style-type: none"> • IBS: 1.65 (+/- 0.03) • Abdominal pain: 1.59 (+/- 0.06) • Constipation: 1.55 (+/- 0.09) • Diarrhea: 2.01 (+/- 1.26)* <p>* P<0.05 vs IBS</p> <p>Sensitivity (yellow) and specificity (blue) of Rome II was largely unchanged by excluding patients with alarm features</p> <p>R Whitehead WE et al. <i>Aliment Pharmacol Ther</i> 2006; 24:137 D70</p>																								
<p>D71</p>	<p>Diagnostic Strength of Red Flags in IBS</p>	<p>Diagnostic Strength of Red Flags in IBS</p> <table border="1"> <thead> <tr> <th>Red Flag</th> <th>OR (95% CI)</th> </tr> </thead> <tbody> <tr> <td>Rectal bleeding</td> <td>0.62 (0.41-0.94)</td> </tr> <tr> <td>Increased ESR</td> <td>3.57 (2.54-5.02)</td> </tr> <tr> <td>+ FOB</td> <td>1.83 (0.55-6.14)</td> </tr> <tr> <td>Rectal bleeding</td> <td>1.26 (0.47-3.39)</td> </tr> <tr> <td>Weight loss</td> <td>0.77 (0.11-5.52)</td> </tr> <tr> <td>Nocturnal diarrhea</td> <td>0.93 (0.46-1.89)</td> </tr> <tr> <td>Nocturnal BM</td> <td>1.12 (0.2-6.19)</td> </tr> <tr> <td>Nocturnal pain</td> <td>2.22 (0.35-14.03)</td> </tr> <tr> <td>Nocturnal symptoms</td> <td>1.55 (0.52-4.58)</td> </tr> <tr> <td>Severe pain</td> <td>1.4 (0.7-2.56)</td> </tr> <tr> <td>Summary OR</td> <td>0.93 (0.55-1.59)</td> </tr> </tbody> </table> <p>1.0 Neutral predictive value</p> <p>R Ganguli SC et al. <i>Neurogastroenterol Motil</i>. 2004; 16:666 D71</p>	Red Flag	OR (95% CI)	Rectal bleeding	0.62 (0.41-0.94)	Increased ESR	3.57 (2.54-5.02)	+ FOB	1.83 (0.55-6.14)	Rectal bleeding	1.26 (0.47-3.39)	Weight loss	0.77 (0.11-5.52)	Nocturnal diarrhea	0.93 (0.46-1.89)	Nocturnal BM	1.12 (0.2-6.19)	Nocturnal pain	2.22 (0.35-14.03)	Nocturnal symptoms	1.55 (0.52-4.58)	Severe pain	1.4 (0.7-2.56)	Summary OR	0.93 (0.55-1.59)
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<p>D72</p>	<p>Investigation in Patients With No Alarm Features</p>	<p>Investigation in Patients With No Alarm Features</p> <ul style="list-style-type: none"> • Flexible sigmoidoscopy • Colonoscopy • Rectal biopsy • Barium enema • Abdominal ultrasound • Routine laboratory investigations • Fecal occult blood test • Serological tests for celiac disease → May be considered* <p>Insufficient evidence to recommend routine testing*</p> <p>Routine use of colonoscopy for CRC screening is recommended for all patients ≥50 years old * Results based on a literature review</p> <p>Cash BD et al. <i>Am J Gastroenterol</i>. 2002; 97:2812 Brandt LJ et al. <i>Am J Gastroenterol</i>. 2005; 100(Suppl.1):S5 R D72</p>																								


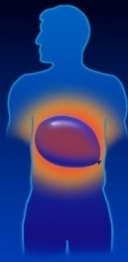
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<p>D73</p>	<p>Diagnostic Cost of Excluding Red Flags</p>	<p>Diagnostic Cost of Excluding Red Flags</p> <table border="1"> <caption>Diagnostic Cost of Excluding Red Flags</caption> <thead> <tr> <th># Red Flags Reported</th> <th>% Missed IBS diagnoses</th> </tr> </thead> <tbody> <tr> <td>7 1</td> <td>~85</td> </tr> <tr> <td>7 2</td> <td>~45</td> </tr> <tr> <td>7 3</td> <td>~20</td> </tr> <tr> <td>7 4</td> <td>~10</td> </tr> <tr> <td>7 5</td> <td>~5</td> </tr> <tr> <td>6</td> <td>~2</td> </tr> <tr> <td>All exs</td> <td>~1</td> </tr> </tbody> </table> <p>Whitehead WE et al. <i>Aliment Pharmacol Ther</i>. 2006; 24:137</p>	# Red Flags Reported	% Missed IBS diagnoses	7 1	~85	7 2	~45	7 3	~20	7 4	~10	7 5	~5	6	~2	All exs	~1
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<p>D74</p>	<p>Stool Form Depends on Water Content and Correlates With Transit Time</p>	<p>Diagnosis Stool Form Depends on Water Content and Correlates With Transit Time</p> <p>Lewis SJ, Heaton KW. <i>Scand J Gastroenterol</i> 1997; 32:920 Heaton KW, O'Donnell LJ. <i>J Clin Gastroenterol</i> 1994; 19:28</p>																
<p>D75</p>	<p>IBS Subtypes</p>	<p>IBS Subtypes: Stool Form is the Differentiating Factor</p> <p>25% of BM is the threshold for classification</p> <p>IBS-C, IBS-M, IBS-U, IBS-D</p> <p>Bristol types 1 and 2, Bristol types 1 and 6, Bristol types 6</p>																



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<p>D76</p>	<p>IBS Subtypes: Stool Form is the Differentiating Factor</p>	<p>IBS Subtypes: Stool Form is the Differentiating Factor</p> <p>25% of BM is the threshold for classification</p> <p>% BM hard or lumpy</p> <p>% BM loose or watery</p> <p>IBS-C, IBS-M, IBS-U, IBS-D</p> <p>Bristol types 1 and 2, Bristol types 1 and 6, Bristol types 6</p> <p>R <small>D76</small></p>
<p>D77</p>	<p>Proposed Pathophysiology of IBS</p>	<p>Proposed Pathophysiology of IBS</p> <p>Genetic factors, Environment, Acute gastroenteritis, Other precipitating factors</p> <p>Gastrointestinal motor disturbances: Enteric neuropathy, Visceral hypersensitivity, Abnormal central processing of sensations, Psychological disturbances</p> <p>Food, Stress</p> <p>Symptoms</p> <p>Consultation</p> <p>R <small>D77</small></p>
<p>D78</p>	<p>Multiple Contributing Factors for IBS</p>	<p>Multiple Contributing Factors for IBS</p> <p>Postinfectious, Visceral hypersensitivity, GI dysmotility, Genetic predisposition, Food sensitivity, Abnormal central processing, Brain-gut dysfunction, Environmental factors, Inflammation, Psychological abuse history</p> <p>IBS Symptom Complex</p> <p>R <small>D78</small></p>

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<p>D79</p>	<p>Natural History of IBS</p>	<p>Natural History of IBS</p> <ul style="list-style-type: none"> 6 months–6 years after original IBS diagnosis <table border="1"> <thead> <tr> <th colspan="2">Patients with IBS diagnosis (%)</th> </tr> </thead> <tbody> <tr> <td>Alternative diagnosis</td> <td>2–5</td> </tr> <tr> <td>Worsened IBS symptoms</td> <td>2–18</td> </tr> <tr> <td>Symptom-free</td> <td>12–38</td> </tr> <tr> <td>Unchanged IBS symptoms</td> <td>30–50</td> </tr> </tbody> </table> <p><small>Total n=1099; 14 studies included</small></p> <ul style="list-style-type: none"> IBS is a stable diagnosis <5% IBS patients are diagnosed with an alternative organic GI disorder; repeated diagnostic evaluation is not warranted <p><small>El-Serafi HB et al. Alliment Pharmacol Ther. 2004; 19:861</small></p> <p><small>D79</small></p>	Patients with IBS diagnosis (%)		Alternative diagnosis	2–5	Worsened IBS symptoms	2–18	Symptom-free	12–38	Unchanged IBS symptoms	30–50
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<p>D80</p>	<p>Pragmatic Issues in IBS</p>	<p>Pragmatic Issues in IBS</p>  <ul style="list-style-type: none"> Patient expectations Effect on clinical outcomes Reassurance value / Impact on symptoms Legal implications of delayed diagnosis of organic GI disease <p><small>D80</small></p>										
<p>D81</p>	<p>Functional Bloating: Diagnostic Criteria</p>	<p>Functional Bloating: Diagnostic Criteria*</p>  <p>Must include all of the following:</p> <ul style="list-style-type: none"> Recurrent feeling of bloating or visible distention at least 3 days/month in 3 months There are insufficient criteria for a diagnosis of functional dyspepsia, irritable bowel syndrome, or other functional GI disorder <p><small>* Criteria fulfilled for the last 3 months with symptom onset 6 months prior to diagnosis</small></p> <p><small>D81</small></p>										

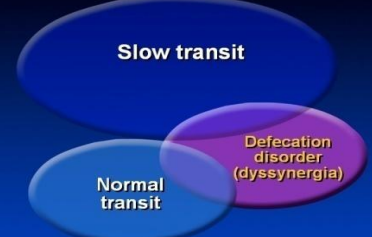
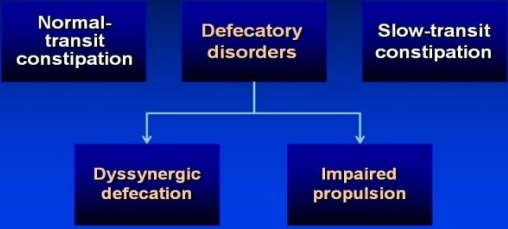

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<p>D82</p>	<p>Primary Constipation Syndromes</p>	<p>Primary Constipation Syndromes</p>  <p>Normal transit Slow transit</p> <p><small>℞ Schiller LR. Aliment Pharmacol Ther. 2001; 15:749 Mertz H et al. Am J Gastroenterol. 1999; 94:609</small></p> <p style="text-align: right;"><small>D82</small></p>																											
<p>D83</p>	<p>Overlap Between Chronic Constipation and IBS With Constipation</p>	<p>Diagnosis</p> <p>Overlap Between Chronic Constipation and IBS With Constipation</p>  <p>Abdominal Pain / Discomfort +</p> <p>Chronic constipation IBS with constipation</p> <p><small>℞</small></p> <p style="text-align: right;"><small>D83</small></p>																											
<p>D84</p>	<p>Supporting Symptoms for IBS-C and Chronic Constipation</p>	<p>Diagnosis</p> <p>Supporting Symptoms</p> <table border="1" data-bbox="1396 966 1879 1193"> <thead> <tr> <th></th> <th>IBS-C</th> <th>CC</th> </tr> </thead> <tbody> <tr> <td>Abdominal pain / discomfort</td> <td>+++</td> <td>+/-</td> </tr> <tr> <td>Bloating / abdominal distension</td> <td>+++</td> <td>++</td> </tr> <tr> <td>Sense of anorectal obstruction</td> <td>+</td> <td>+++</td> </tr> <tr> <td>Manual maneuvers</td> <td>+</td> <td>+++</td> </tr> <tr> <td><3 BMs / week</td> <td>+++</td> <td>+++</td> </tr> <tr> <td>Hard / lumpy stools</td> <td>+++</td> <td>+++</td> </tr> <tr> <td>Straining</td> <td>+++</td> <td>+++</td> </tr> <tr> <td>Feeling of incomplete evacuation</td> <td>+++</td> <td>+++</td> </tr> </tbody> </table> <p><small>¹Drossman DA et al. Gastroenterology. 1997; 112:2120 ²Thompson WG et al. Gut. 1999; 45(Suppl. 2):II43</small></p> <p><small>℞</small></p> <p style="text-align: right;"><small>D84</small></p>		IBS-C	CC	Abdominal pain / discomfort	+++	+/-	Bloating / abdominal distension	+++	++	Sense of anorectal obstruction	+	+++	Manual maneuvers	+	+++	<3 BMs / week	+++	+++	Hard / lumpy stools	+++	+++	Straining	+++	+++	Feeling of incomplete evacuation	+++	+++
	IBS-C	CC																											
Abdominal pain / discomfort	+++	+/-																											
Bloating / abdominal distension	+++	++																											
Sense of anorectal obstruction	+	+++																											
Manual maneuvers	+	+++																											
<3 BMs / week	+++	+++																											
Hard / lumpy stools	+++	+++																											
Straining	+++	+++																											
Feeling of incomplete evacuation	+++	+++																											


Computer-Based Learning Program
Diagnosis

<p>D85</p>	<p>BM Infrequency Is Not the Defining Symptom</p>	<p>Diagnosis: Chronic Constipation</p> <p>BM Infrequency Is Not the Defining Symptom</p> <p> <small> Pare P et al. Am J Gastroenterol. 2001; 96:3131 </small> </p> <p style="text-align: right;"><small>D85</small></p>																		
<p>D86</p>	<p>ACG Task Force Recommendations on Diagnostic Testing for CC</p>	<p>ACG Task Force Recommendations on Diagnostic Testing for CC</p> <ul style="list-style-type: none"> • No alarm features ... little yield “The routine approach to a patient with symptoms of chronic constipation without alarm signs or symptoms should be empiric treatment without performance of diagnostic testing” • Diagnostic studies are indicated in patients with alarm signs or symptoms • Routine colon cancer screening recommended in patients aged ≥ 50 years (African Americans aged ≥ 45 years) <p> <small> ACG = American College of Gastroenterology Brandt LJ et al. Am J Gastroenterol. 2005; 100(Suppl 1):S5 Agrawal S et al. Am J Gastroenterol. 2005; 100:515 </small> </p> <p style="text-align: right;"><small>D86</small></p>																		
<p>D87</p>	<p>Some Causes of Secondary Constipation</p>	<p>Some Causes of Secondary Constipation</p> <table border="0"> <tr> <td>Endocrine and metabolic</td> <td>→</td> <td>Diabetes, thyroid disorders, hypercalcemia</td> </tr> <tr> <td>Neurologic</td> <td>→</td> <td>Spinal cord injury, multiple sclerosis, Parkinson's disease, cerebrovascular accident, Hirschprung's disease</td> </tr> <tr> <td>Anorectal</td> <td>→</td> <td>Anal fissures and strictures</td> </tr> <tr> <td>Psychogenic</td> <td>→</td> <td>Depression, eating disorders</td> </tr> <tr> <td>Iatrogenic</td> <td>→</td> <td>Drugs, surgery</td> </tr> <tr> <td>Dietary/lifestyle</td> <td>→</td> <td>Low-residue diet</td> </tr> </table> <p> <small> R </small> </p> <p style="text-align: right;"><small>D87</small></p>	Endocrine and metabolic	→	Diabetes, thyroid disorders, hypercalcemia	Neurologic	→	Spinal cord injury, multiple sclerosis, Parkinson's disease, cerebrovascular accident, Hirschprung's disease	Anorectal	→	Anal fissures and strictures	Psychogenic	→	Depression, eating disorders	Iatrogenic	→	Drugs, surgery	Dietary/lifestyle	→	Low-residue diet
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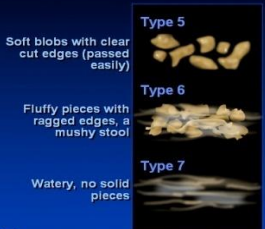
Computer-Based Learning Program
Diagnosis

D88	Primary Constipation Syndromes	<p>Primary Constipation Syndromes</p>  <p>Slow transit</p> <p>Normal transit</p> <p>Defecation disorder (dyssynergia)</p> <p><small>Schiller LR. Aliment Pharmacol Ther. 2001; 15:749 Mertz H et al. Am J Gastroenterol. 1999; 94:609</small></p> <p>R D88</p>
D89	Conceptual Categorization of Constipation	<p>Conceptual Categorization of Constipation</p>  <p>Normal-transit constipation</p> <p>Defecatory disorders</p> <p>Slow-transit constipation</p> <p>Dyssynergic defecation</p> <p>Impaired propulsion</p> <p>R D89</p>
D90	Colonic Transit Study (Hinton Technique)	<p>Diagnostic Tests</p> <p>Colonic Transit Study (Hinton Technique)</p>  <ul style="list-style-type: none">• Measures rate at which fecal residue moves through colon• The patient swallows a capsule filled with 24 radiopaque markers• Abdominal radiograph is taken 120 hours later• Normal <5 markers on day 5 <p><small>Hinton JM et al. Gut 1969; 10:842</small></p> <p>R D90</p>


Computer-Based Learning Program
Diagnosis

<p>D91</p>	<p>Colonic Transit Study (Metcalf Technique)</p>	<p>Diagnostic Tests</p> <p>Colonic Transit Study (Metcalf Technique)</p> <ul style="list-style-type: none"> • Ingest 24 radiopaque markers on 3 successive days • No laxatives, enemas, or medicines that affect bowel function • Days 4 and 7: abdominal x-ray • Colonic transit = markers (on days 4 and 7), normal <70 markers  <p><small>Metcalf AM et al. Gastroenterology 1987; 92:40</small></p> <p>D91</p>								
<p>D92</p>	<p>Constipation: Diagnostic Algorithm</p>	<p>Constipation: Diagnostic Algorithm</p> <p>History / Physical exam</p> <p>Alarm symptoms Weight loss, blood in stool, >50 years of age, etc.</p> <p>No → Investigate and treat</p> <p>Yes → Investigate and treat</p> <table border="1"> <tr> <td>Abdominal pain +++</td> <td>Abdominal pain +/-</td> </tr> <tr> <td>Bloating +++</td> <td>Bloating ++</td> </tr> <tr> <td></td> <td>Sense of anorectal obstruction +</td> </tr> <tr> <td></td> <td>Manual maneuvers +</td> </tr> </table> <p>IBS-C CC</p> <p>Investigate and treat</p> <p>If no improvement → Re-evaluate diagnosis and treatment strategy Consider referral to specialist</p> <p><small>Schiller LR. Aliment Pharmacol Ther. 2001; 15:749</small></p> <p>D92</p>	Abdominal pain +++	Abdominal pain +/-	Bloating +++	Bloating ++		Sense of anorectal obstruction +		Manual maneuvers +
Abdominal pain +++	Abdominal pain +/-									
Bloating +++	Bloating ++									
	Sense of anorectal obstruction +									
	Manual maneuvers +									
<p>D93</p>	<p>Primary Constipation Syndromes: Coexistent Slow Colonic Transit and Defecation Disorder</p>	<p>Primary Constipation Syndromes: Coexistent Slow Colonic Transit and Defecation Disorder</p> <p>After biofeedback with persistent symptoms</p> <p>Pretreatment</p> <p>Defecation disorder (dyssynergia)</p> <p>Slow transit</p> <p>Biofeedback</p> <p>Normal transit</p> <p>Slow transit</p> <p><small>Schiller LR. Aliment Pharmacol Ther. 2001; 15:749</small></p> <p><small>Mertz H et al. Am J Gastroenterol. 1999; 94:609</small></p> <p>D93</p>								


Computer-Based Learning Program
Diagnosis

<p>D94</p>	<p>Functional Diarrhea: Diagnostic Criteria</p>	<p>Functional Diarrhea: Diagnostic Criteria*</p>  <ul style="list-style-type: none"> • Loose (mushy) or watery stools without pain occurring for at least 75% of stools <p>* Criteria fulfilled for the last 3 months with symptom onset 6 months prior to diagnosis</p>
<p>D95</p>	<p>Evaluation of Functional Diarrhea: History</p>	<p>Evaluation of Functional Diarrhea: History</p> <p>Careful history</p> <ul style="list-style-type: none"> • 75% rule <ul style="list-style-type: none"> • Intermittent constipation, abdominal pain suggest IBS • Dietary history <ul style="list-style-type: none"> • Carbohydrates, alcohol • Alarm features <ul style="list-style-type: none"> • Weight loss, nocturnal symptoms, tenesmus, recent abx, family history of GI disease, hematochezia, high-volume (250 cc/day) diarrhea, physical exam abnormalities (clubbing, abdominal masses, or tenderness)
<p>D96</p>	<p>Evaluation of Functional Diarrhea: Diagnostic Testing</p>	<p>Evaluation of Functional Diarrhea: Diagnostic Testing</p> <p>Diagnostic Tests: Diagnostic Yield Unproven</p> <ul style="list-style-type: none"> • Labs: CBC, ESR, electrolytes, albumin, celiac disease abs, TFTs, stool studies (electrolytes, O&P, fecal fat) <p>More than one abnormality suggests organic disease</p> <ul style="list-style-type: none"> • Endoscopy: Proctosigmoidoscopy, colonoscopy, ileoscopy, capsule endoscopy • Radiographs: small-intestinal radiographs, SBFT

Computer-Based Learning Program
Diagnosis

<p>D97</p>	<p>Differential Diagnosis for Functional Diarrhea</p>	<p>Diagnosis</p> <p>Differential Diagnosis for Functional Diarrhea</p>  <p>R</p> <p>D97</p>
<p>D98</p>	<p>Functional Abdominal Pain Syndrome: Diagnostic Criteria</p>	<p>Functional Abdominal Pain Syndrome: Diagnostic Criteria*</p> <p>Must include all of the following:</p> <ol style="list-style-type: none"> 1. Continuous or nearly continuous abdominal pain 2. No (or only occasional) relationship of pain with physiological events (eating, defecation, menses) 3. Some loss of daily functioning 4. The pain is not feigned 5. Insufficient symptoms to meet criteria for another functional GI disorder that would explain the pain <p>* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis</p> <p>R</p> <p>Clouse RE et al. <i>Gastroenterology</i>; 2006; 130:1492.</p> <p>D98</p>
<p>D99</p>	<p>Clinical Assessment in FAPS</p>	<p>Clinical Assessment in FAPS</p> <ol style="list-style-type: none"> 1. What is the life history of illness? 2. Why are they presenting now? 3. Is there a history of traumatic life events? 4. What is their understanding of the illness? 5. What is the impact of pain on activities and QOL? 6. Is there an associated psychiatric diagnosis? 7. What is the role of family or culture? 8. What are the patient's psychosocial impairments and resources? <p>R</p> <p>Drossman D. <i>Clin Gastroenterol Hepatol</i>. 2004; 2:353</p> <p>D99</p>

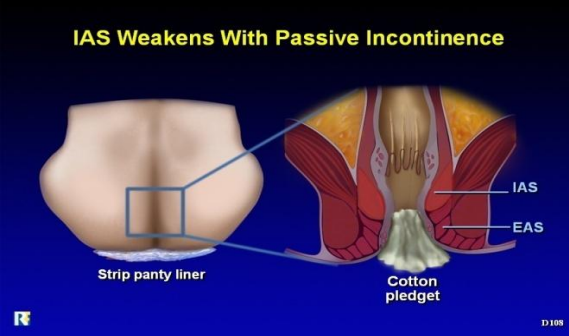
Computer-Based Learning Program
Diagnosis

D100	FAPS: Physical Examination	<p>Physical Examination</p> <ul style="list-style-type: none">• Does not establish a diagnosis of FAPS but is essential; may focus further testing• Abdominal examination<ul style="list-style-type: none">• Surgical scars• "Closed-eyes" sign: Wincing with closed eyes during examination supports FAPS• Stethoscope sign: Pain reduced during auscultation• Fothergill's sign: Increased symptoms with relaxation of the abdomen supports intra-abdominal source• Carnett's test: Pt supine, tenses abdominal muscles<ul style="list-style-type: none">• Pain stable or increases: abdominal wall pain• Digital rectal examination/perineum <p>R The sensitivity and specificity of these tests have not been established <small>Drossman D. Clin Gastroenterol Hepatol. 2004; 2:353 Clouse RE et al. Gastroenterology. 2006; 130:1492</small></p> <p>D100</p>
D101	Functional Anorectal Disorders	<p>Functional Anorectal Disorders</p> <ul style="list-style-type: none">• Functional fecal incontinence• Functional anorectal pain, chronic proctalgia (levator ani syndrome, unspecified anorectal pain), proctalgia fugax• Functional defecation disorders, dyssynergic defecation, inadequate defecatory propulsion <p>R</p> <p>D101</p>
D102	Functional Fecal Incontinence	<p>Functional Fecal Incontinence</p>  <p>Liquid stool seeps around impaction and through anal canal</p> <p>R</p> <p>D102</p>


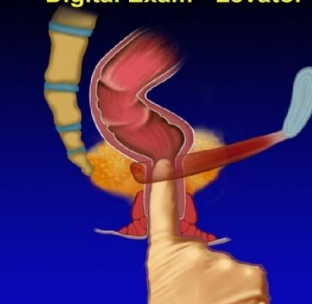
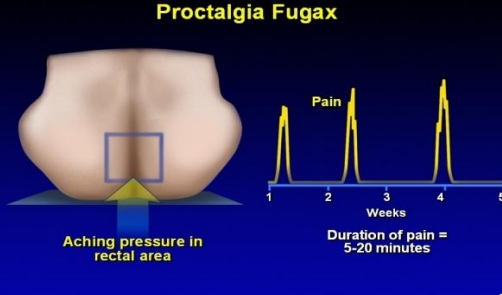
Computer-Based Learning Program
Diagnosis

D103	Digital Exam for Continence-Slide 1 of 5	 <p>Digital Exam for Continence</p> <p>Position 1 Check anal tone at rest</p> <p>Symphysis pubis Puborectalis Internal anal sphincter External anal sphincter (EAS)</p> <p>R D103</p>
D104	Digital Exam for Continence-Slide 2 of 5	 <p>Digital Exam for Continence</p> <p>Position 1 Check anal tone at rest Ask patient to squeeze</p> <p>Symphysis pubis Puborectalis Internal anal sphincter External anal sphincter (EAS)</p> <p>R D104</p>
D105	Digital Exam for Continence-Slide 3 of 5	 <p>Digital Exam for Continence</p> <p>Position 2 Insert finger deeper and feel puborectalis muscle</p> <p>Symphysis pubis Puborectalis Internal anal sphincter External anal sphincter (EAS)</p> <p>R D105</p>


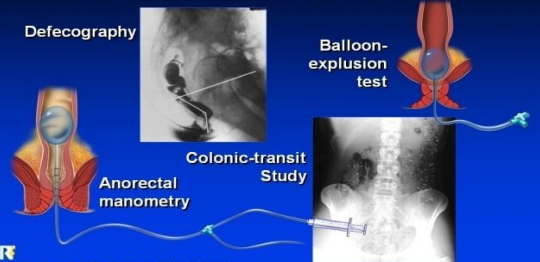

Computer-Based Learning Program
Diagnosis

D106	Digital Exam for Continence-Slide 4 of 5	 <p>Digital Exam for Continence</p> <p>Position 2 Insert finger deeper and feel puborectalis muscle Ask patient to squeeze</p> <p>Labels: Symphysis pubis, Puborectalis, External anal sphincter (EAS), Internal anal sphincter.</p> <p><small>R D106</small></p>
D107	Digital Exam for Continence-Slide 5 of 5	 <p>Digital Exam for Continence</p> <p>Expulsion</p> <p>Puborectalis relaxes Anal canal relaxes Perineum descends Angle widens</p> <p><small>R D107</small></p>
D108	IAS Weakens With Passive Incontinence	 <p>IAS Weakens With Passive Incontinence</p> <p>Strip panty liner Cotton pledget IAS EAS</p> <p><small>R D108</small></p>

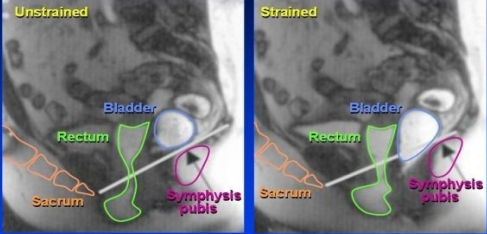
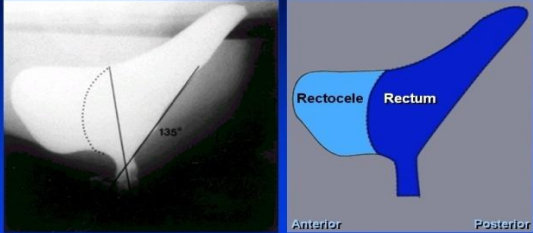
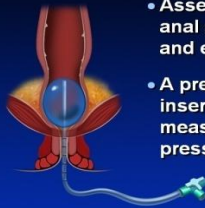
Computer-Based Learning Program
Diagnosis

D109	Digital Exam - Coccygodynia	<p>Digital Exam - Coccygodynia</p>  <ul style="list-style-type: none">• Squeeze coccyx between forefinger and thumb• Tenderness suggests diagnosis <p>R D109</p>
D110	Chronic Proctalgia Syndrome	<p>Digital Exam - Levator Syndrome</p>  <ul style="list-style-type: none">• Palpate around the puborectalis• Tenderness suggests diagnosis <p>R D110</p>
D111	Proctalgia Fugax	<p>Proctalgia Fugax</p>  <p>Aching pressure in rectal area</p> <p>Duration of pain = 5-20 minutes</p> <p>R D111</p>

Computer-Based Learning Program
Diagnosis

D112	Primary Constipation Syndromes: Association with Dyssynergia	<p>Primary Constipation Syndromes</p>  <p><i>Schiller LR. Aliment Pharmacol Ther. 2001; 15:749</i> <i>Mertz H et al. Am J Gastroenterol. 1999; 94:609</i></p> <p>D112</p>
D113	Diagnostic Tests for Constipation	<p>Diagnosis</p> <p>Diagnostic Tests for Constipation</p>  <p><i>Lembo A et al. N Engl J Med. 2003; 349:1360</i></p> <p>D113</p>
D114	Defecography	<p>Diagnostic Tests</p> <p>Defecography</p>  <ul style="list-style-type: none">• Detects structural abnormalities of the rectum• Thickened barium is instilled into the rectum• Radiographic films are taken during defecation <p><i>Schiller LR. Aliment Pharmacol Ther. 2001; 15:749</i></p> <p>D114</p>

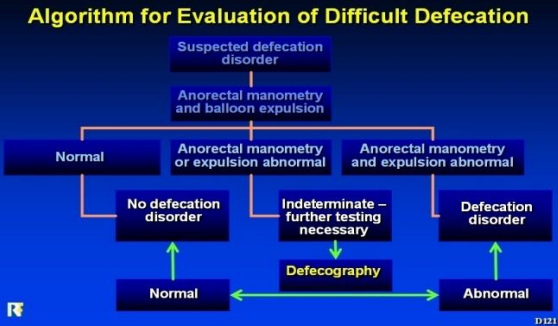
Computer-Based Learning Program
Diagnosis

D115	Pelvic MRI	<p>Diagnostic Tests</p> <h3>Pelvic MRI</h3>  <p>Unstrained</p> <p>Strained</p> <p>Bladder</p> <p>Rectum</p> <p>Sacrum</p> <p>Symphysis pubis</p> <p>R</p> <p>D115</p>
D116	Rectocele	<h3>Rectocele</h3>  <p>Rectocele</p> <p>Rectum</p> <p>Anterior</p> <p>Posterior</p> <p>R</p> <p>D116</p>
D117	Anorectal Manometry	<p>Diagnostic Tests</p> <h3>Anorectal Manometry</h3>  <ul style="list-style-type: none">• Assesses the internal and external anal sphincters, rectal sensations, and expulsion patterns• A pressure-sensitive catheter is inserted into the anorectum to measure resting and squeeze pressures of the anal canal <p>R</p> <p>D117</p>

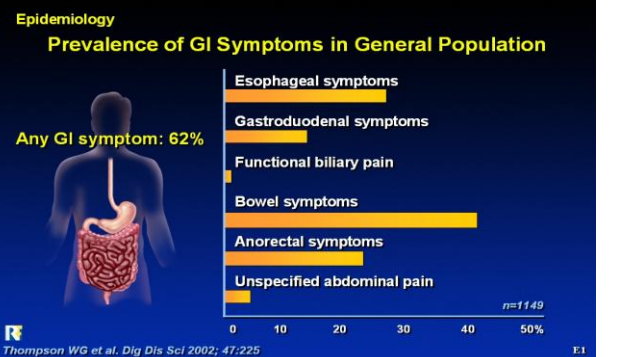

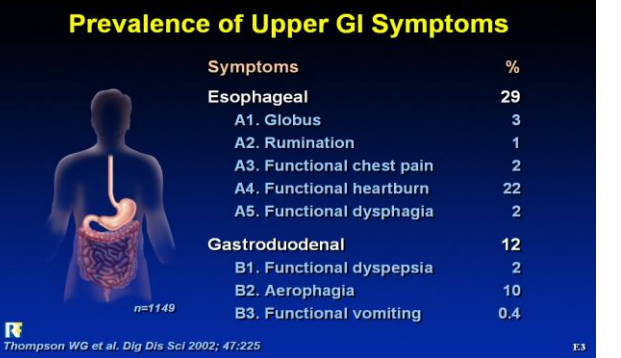
Computer-Based Learning Program
Diagnosis

D118	Rectoanal Pressure Profiles	<p>Diagnosis</p> <h3>Rectoanal Pressure Profiles</h3> <p>Normal Dyssynergia Type I Dyssynergia Type II Inadequate expulsion</p> <p>Rectal mmHg</p> <p>Anal mmHg</p> <p>Rao SS. <i>Gastroenterol Clin N Amer</i> 2003; 32:659</p> <p>D118</p>
D119	Balloon Expulsion Test	<p>Diagnostic Tests</p> <h3>Balloon Expulsion Test</h3> <p>Balloon filled with 50 cc water</p> <p>Anal canal closed</p> <p>Polyethylene catheter</p> <p>3-way stopcock → to pressure transducers</p> <p>Normal < 60 seconds</p> <p>Patient sits on toilet</p> <p>Patient tries to expel balloon</p> <p>Minguez M et al. <i>Gastroenterology</i> 2004; 126:57</p> <p>D119</p>
D120	Balloon Expulsion Device	<h3>Balloon Expulsion Device</h3> <p>Polyethylene tube</p> <p>3-way stopcock</p> <p>Balloon with 50 cc H₂O</p> <p>R</p> <p>D120</p>

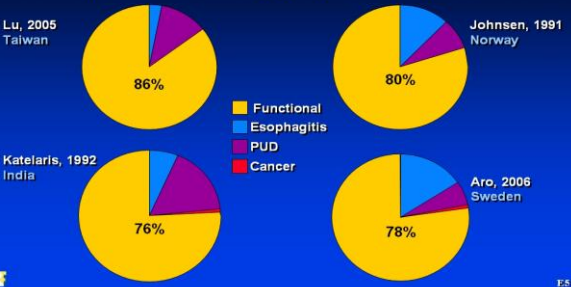
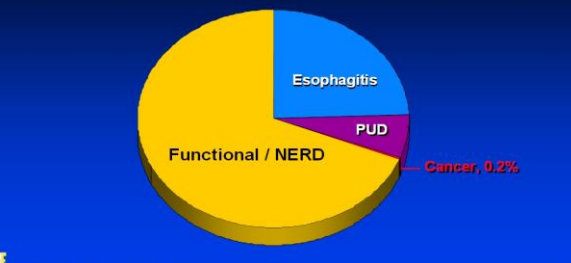
Computer-Based Learning Program
Diagnosis

D121	Algorithm for Evaluation of Difficult Defecation	 <p>The flowchart, titled "Algorithm for Evaluation of Difficult Defecation", outlines the diagnostic pathway. It begins with "Suspected defecation disorder", leading to "Anorectal manometry and balloon expulsion". From here, three paths emerge: 1) "Normal" leads to "No defecation disorder". 2) "Anorectal manometry or expulsion abnormal" leads to "Indeterminate - further testing necessary", which then leads to "Defecography". 3) "Anorectal manometry and expulsion abnormal" leads to "Defecation disorder". The "Defecography" step further branches into "Normal" (which leads back to "No defecation disorder") and "Abnormal" (which leads to "Defecation disorder"). A small "D121" identifier is present in the bottom right corner of the flowchart area.</p>

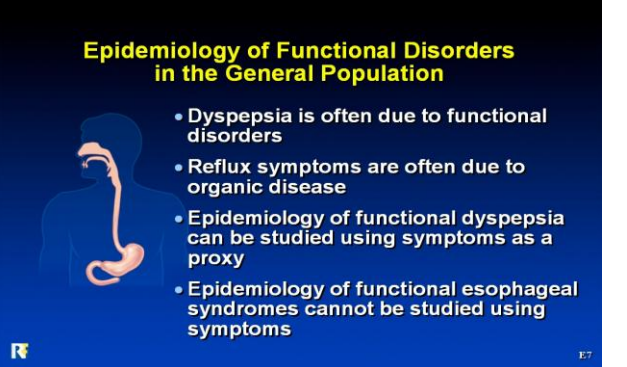
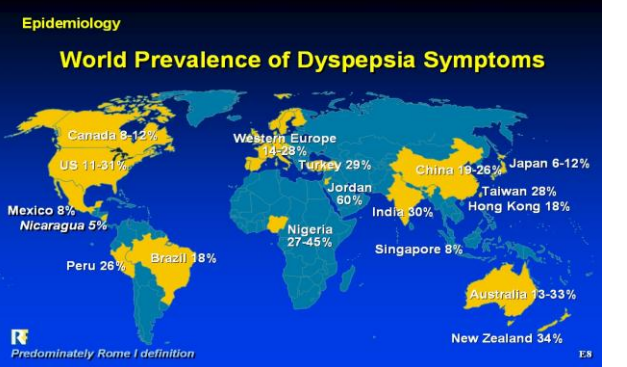
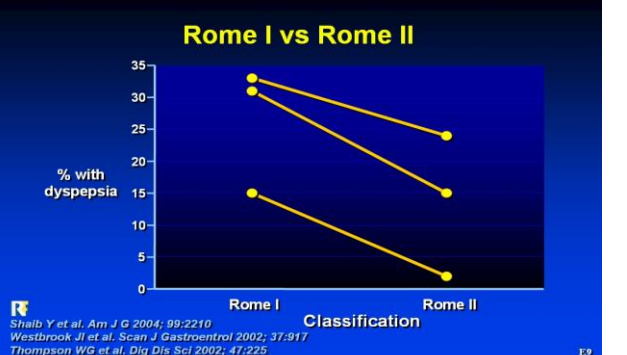
Specialty Modules for Rome Slide Sets Epidemiology

Slide Number	Slide Title	Slide Image																						
E1	Prevalence of GI Symptoms in General Population	 <p>Epidemiology Prevalence of GI Symptoms in General Population</p> <p>Any GI symptom: 62%</p> <table border="1"> <thead> <tr> <th>Symptom</th> <th>Prevalence (%)</th> </tr> </thead> <tbody> <tr> <td>Esophageal symptoms</td> <td>12</td> </tr> <tr> <td>Gastroduodenal symptoms</td> <td>12</td> </tr> <tr> <td>Functional biliary pain</td> <td>2</td> </tr> <tr> <td>Bowel symptoms</td> <td>42</td> </tr> <tr> <td>Anorectal symptoms</td> <td>12</td> </tr> <tr> <td>Unspecified abdominal pain</td> <td>2</td> </tr> </tbody> </table> <p><i>Thompson WG et al. Dig Dis Sci 2002; 47:225</i> E1</p>	Symptom	Prevalence (%)	Esophageal symptoms	12	Gastroduodenal symptoms	12	Functional biliary pain	2	Bowel symptoms	42	Anorectal symptoms	12	Unspecified abdominal pain	2								
Symptom	Prevalence (%)																							
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E2	Prevalence	 <p>Epidemiology Prevalence</p> <ul style="list-style-type: none"> • IBS, constipation, diarrhea, dyspepsia, and GERS: <ul style="list-style-type: none"> • All are common • 62% report symptoms • If you are symptom-free, you are in the minority! <p><i>Thompson WG et al. Dig Dis Sci 2002; 47:225</i> E2</p>																						
E3	Prevalence of Upper GI Symptoms	 <p>Prevalence of Upper GI Symptoms</p> <table border="1"> <thead> <tr> <th>Symptoms</th> <th>%</th> </tr> </thead> <tbody> <tr> <td>Esophageal</td> <td>29</td> </tr> <tr> <td>A1. Globus</td> <td>3</td> </tr> <tr> <td>A2. Rumination</td> <td>1</td> </tr> <tr> <td>A3. Functional chest pain</td> <td>2</td> </tr> <tr> <td>A4. Functional heartburn</td> <td>22</td> </tr> <tr> <td>A5. Functional dysphagia</td> <td>2</td> </tr> <tr> <td>Gastroduodenal</td> <td>12</td> </tr> <tr> <td>B1. Functional dyspepsia</td> <td>2</td> </tr> <tr> <td>B2. Aerophagia</td> <td>10</td> </tr> <tr> <td>B3. Functional vomiting</td> <td>0.4</td> </tr> </tbody> </table> <p><i>Thompson WG et al. Dig Dis Sci 2002; 47:225</i> E3</p>	Symptoms	%	Esophageal	29	A1. Globus	3	A2. Rumination	1	A3. Functional chest pain	2	A4. Functional heartburn	22	A5. Functional dysphagia	2	Gastroduodenal	12	B1. Functional dyspepsia	2	B2. Aerophagia	10	B3. Functional vomiting	0.4
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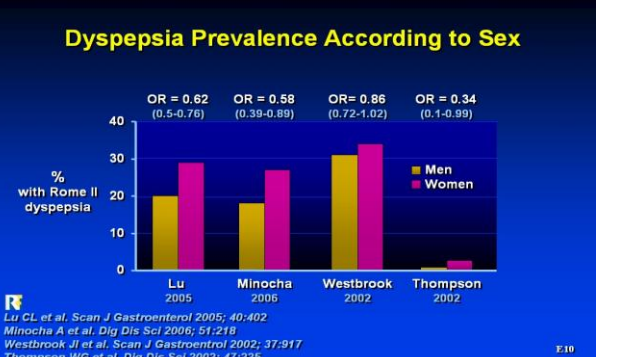
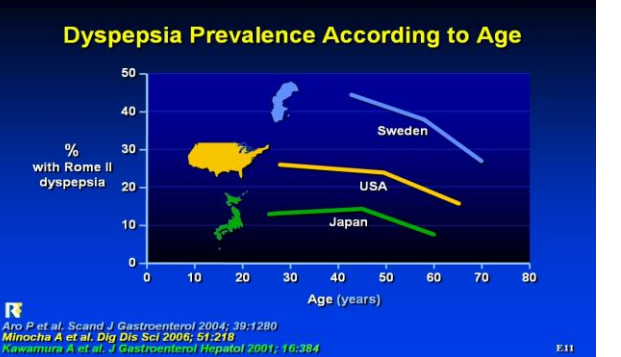
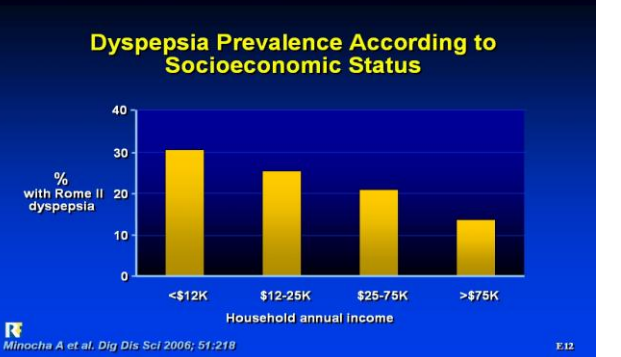
**Specialty Modules for
Rome Slide Sets
Epidemiology**

Slide Number	Slide Title	Slide Image
E4	Definitional Problems with Studies of Upper GI Symptoms	<p style="text-align: center;">Definitional Problems with Studies of Upper GI Symptoms</p> <ul style="list-style-type: none"> • Symptoms are not always defined precisely • Symptoms are usually multiple • Symptom complex may be unclassifiable • Functional status requires endoscopy <ul style="list-style-type: none"> • Organic esophageal pathology are common in West • Organic gastroduodenal pathology are rare in West <p><small>R E4</small></p>
E5	Results of Endoscopy in the General Population with Dyspepsia Symptoms	<p style="text-align: center;">Results of Endoscopy in the General Population with Dyspepsia Symptoms</p>  <p><small>R E5</small></p>
E6	Results of Endoscopy in the General Population with Reflux Symptoms	<p style="text-align: center;">Results of Endoscopy in the General Population with Reflux Symptoms</p>  <p><small>R Ronkalnen J et al. Scand J Gastroenterol 2005; 40: 275 E6</small></p>

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Slide Number	Slide Title	Slide Image
E7	Epidemiology of Functional Disorders in the General Population	 <p style="text-align: center;">Epidemiology of Functional Disorders in the General Population</p> <ul style="list-style-type: none"> • Dyspepsia is often due to functional disorders • Reflux symptoms are often due to organic disease • Epidemiology of functional dyspepsia can be studied using symptoms as a proxy • Epidemiology of functional esophageal syndromes cannot be studied using symptoms
E8	World Prevalence of Dyspepsia Symptoms	 <p style="text-align: center;">Epidemiology World Prevalence of Dyspepsia Symptoms</p> <p><i>Predominately Rome I definition</i></p>
E9	Rome I vs Rome II	 <p style="text-align: center;">Rome I vs Rome II</p> <p>Classification</p> <p><i>Shaib Y et al. Am J G 2004; 99:2210 Westbrook JI et al. Scan J Gastroentrol 2002; 37:917 Thompson WG et al. Dig Dis Sci 2002; 47:225</i></p>

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E11	Dyspepsia Prevalence According to Age	 <p>Dyspepsia Prevalence According to Age</p> <p>Aro P et al. <i>Scand J Gastroenterol</i> 2004; 39:1280 Minocha A et al. <i>Dig Dis Sci</i> 2006; 51:218 Kawamura A et al. <i>J Gastroenterol Hepatol</i> 2001; 16:384</p>																									
E12	Dyspepsia Prevalence According to Socioeconomic Status	 <p>Dyspepsia Prevalence According to Socioeconomic Status</p> <table border="1"> <thead> <tr> <th>Household annual income</th> <th>% with Rome II dyspepsia</th> </tr> </thead> <tbody> <tr> <td><\$12K</td> <td>~30</td> </tr> <tr> <td>\$12-25K</td> <td>~25</td> </tr> <tr> <td>\$25-75K</td> <td>~20</td> </tr> <tr> <td>>\$75K</td> <td>~13</td> </tr> </tbody> </table> <p>Minocha A et al. <i>Dig Dis Sci</i> 2006; 51:218</p>	Household annual income	% with Rome II dyspepsia	<\$12K	~30	\$12-25K	~25	\$25-75K	~20	>\$75K	~13															
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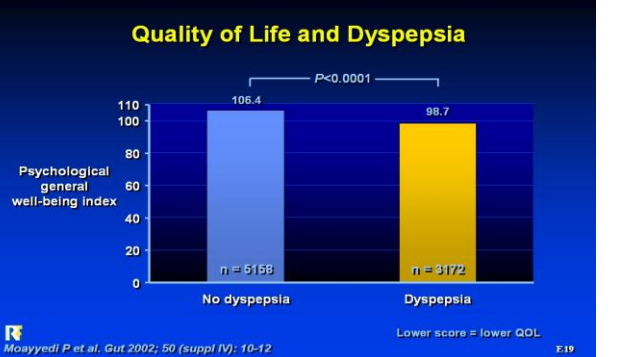
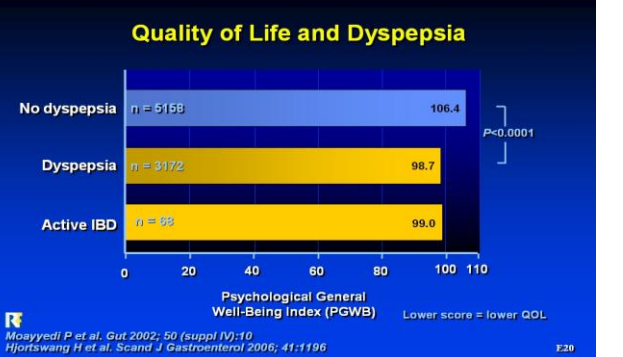
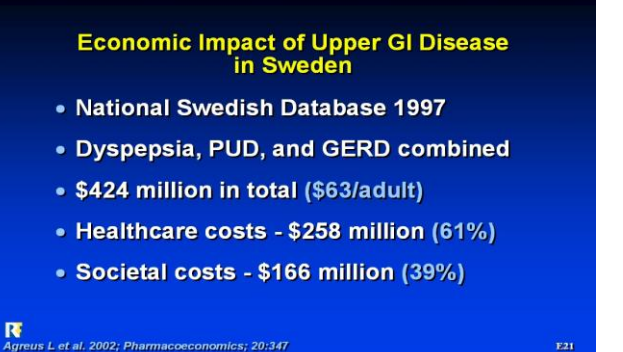
Specialty Modules for Rome Slide Sets Epidemiology

Slide Number	Slide Title	Slide Image																														
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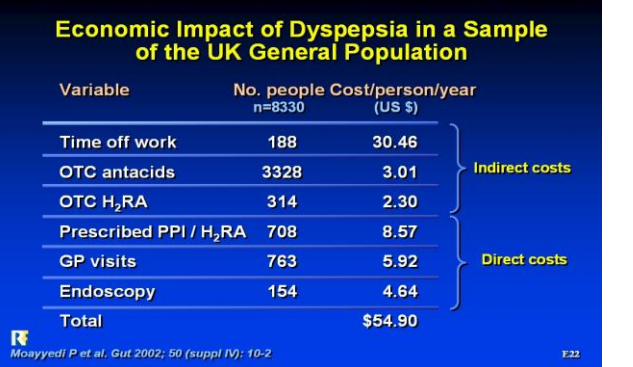
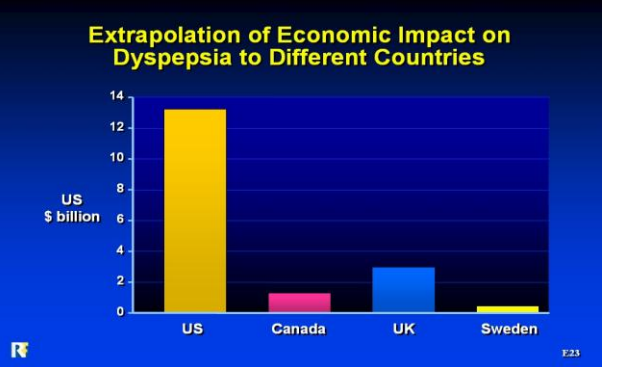
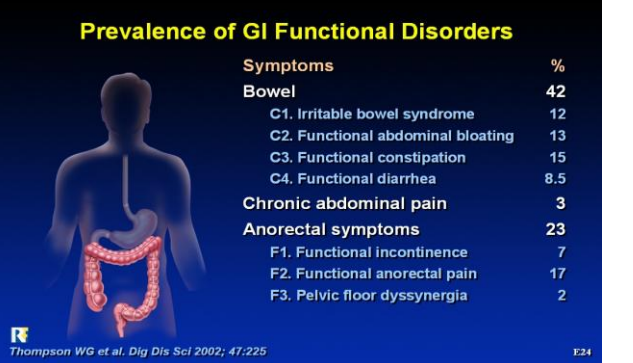
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Slide Number	Slide Title	Slide Image
E16	Incidence of Dyspepsia in the UK General Population, Age 40 to 49 Years-Slide 1 of 2	<p>Incidence of Dyspepsia in the UK General Population, Age 40 to 49 Years</p> <p>At baseline: Dyspepsia 795 (20%), No dyspepsia 3117 (80%).</p> <p>10 years follow-up: Dyspepsia 569 (18%), No dyspepsia 2548 (82%).</p> <p><small>Ford AC et al. Gut 2007; 56:321 Rome II definition of dyspepsia E16</small></p>
E17	Prognosis of Dyspepsia in the General Population-Slide 2 of 2	<p>Prognosis of Dyspepsia in the General Population</p> <p>At baseline: No dyspepsia 3117 (80%), Dyspepsia 795 (20%).</p> <p>10 years follow-up: No dyspepsia 472 (59%), Dyspepsia 323 (41%).</p> <p><small>Ford AC et al. Gut 2007; 56:321 Rome II definition of dyspepsia E17</small></p>
E18	Quality of Life in the US and UK General Population in Those With and Without Dyspepsia	<p>Quality of Life in the US and UK General Population in Those With and Without Dyspepsia</p> <p>Legend: No dyspepsia (blue), Dyspepsia (yellow).</p> <p>Domains: Physical function, Role limitations - physical, Bodily pain, General health, Vitality, Social functioning, Role limitations - emotional, Mental health.</p> <p>$P < 0.05$ (for Physical function, Role limitations - physical, Bodily pain, General health, Vitality, Social functioning, Role limitations - emotional).</p> <p><small>Haider SLS et al. Aliment Pharmacol Ther. 2004; 19:233 Lower score = lower QOL E18</small></p>

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E19	Quality of Life and Dyspepsia	 <p>Quality of Life and Dyspepsia</p> <table border="1"> <thead> <tr> <th>Group</th> <th>n</th> <th>PGWB Score</th> </tr> </thead> <tbody> <tr> <td>No dyspepsia</td> <td>5159</td> <td>106.4</td> </tr> <tr> <td>Dyspepsia</td> <td>3172</td> <td>98.7</td> </tr> </tbody> </table> <p><i>Moayyedi P et al. Gut 2002; 50 (suppl IV): 10-12</i> E19</p>	Group	n	PGWB Score	No dyspepsia	5159	106.4	Dyspepsia	3172	98.7			
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E21	Economic Impact of Upper GI Disease in Sweden	 <p>Economic Impact of Upper GI Disease in Sweden</p> <ul style="list-style-type: none"> • National Swedish Database 1997 • Dyspepsia, PUD, and GERD combined • \$424 million in total (\$63/adult) • Healthcare costs - \$258 million (61%) • Societal costs - \$166 million (39%) <p><i>Agreus L et al. 2002; Pharmacoeconomics; 20:347</i> E21</p>												

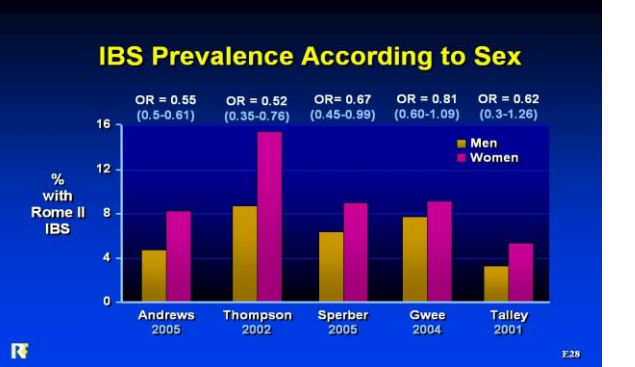
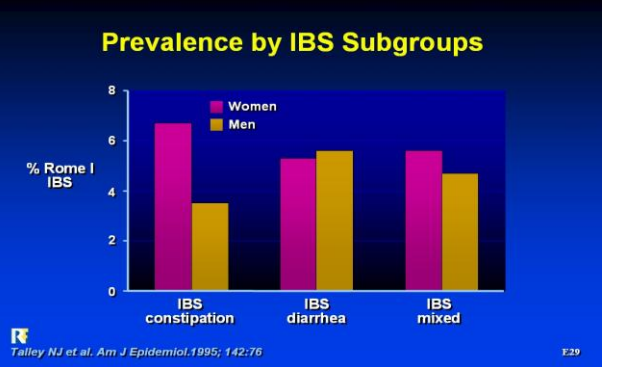
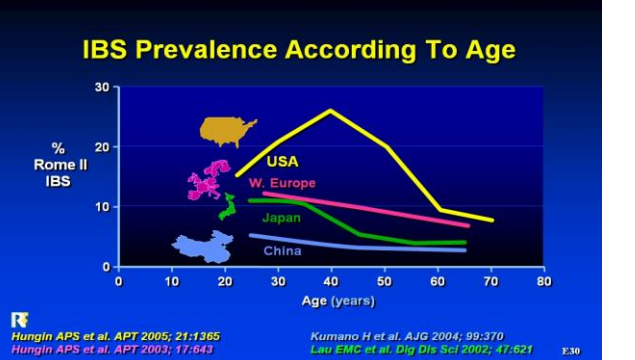
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E22	Economic Impact of Dyspepsia in a Sample of the UK General Population	 <p>Economic Impact of Dyspepsia in a Sample of the UK General Population</p> <table border="1"> <thead> <tr> <th>Variable</th> <th>No. people n=8330</th> <th>Cost/person/year (US \$)</th> <th></th> </tr> </thead> <tbody> <tr> <td>Time off work</td> <td>188</td> <td>30.46</td> <td rowspan="2">} Indirect costs</td> </tr> <tr> <td>OTC antacids</td> <td>3328</td> <td>3.01</td> </tr> <tr> <td>OTC H₂RA</td> <td>314</td> <td>2.30</td> <td rowspan="4">} Direct costs</td> </tr> <tr> <td>Prescribed PPI / H₂RA</td> <td>708</td> <td>8.57</td> </tr> <tr> <td>GP visits</td> <td>763</td> <td>5.92</td> </tr> <tr> <td>Endoscopy</td> <td>154</td> <td>4.64</td> </tr> <tr> <td>Total</td> <td></td> <td>\$54.90</td> <td></td> </tr> </tbody> </table> <p><small>Moayyedi P et al. Gut 2002; 50 (suppl IV): 10-2</small></p>	Variable	No. people n=8330	Cost/person/year (US \$)		Time off work	188	30.46	} Indirect costs	OTC antacids	3328	3.01	OTC H ₂ RA	314	2.30	} Direct costs	Prescribed PPI / H ₂ RA	708	8.57	GP visits	763	5.92	Endoscopy	154	4.64	Total		\$54.90	
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E25	Prevalence of Bowel Habits in US IBS Populations	<p>Epidemiology Prevalence of Bowel Habits in US IBS Populations</p> <table border="1"> <thead> <tr> <th>Bowel Habit</th> <th>Prevalence (%)</th> </tr> </thead> <tbody> <tr> <td>Constipation</td> <td>~25</td> </tr> <tr> <td>Diarrhea</td> <td>~35</td> </tr> <tr> <td>Mixed</td> <td>~20</td> </tr> </tbody> </table> <p><small>Drossman DA et al. Gastroenterology 2005; 128:580 Andrews EB et al. Aliment Pharmacol Ther 2005; 22:935</small></p> <p style="text-align: right;"><small>E25</small></p>	Bowel Habit	Prevalence (%)	Constipation	~25	Diarrhea	~35	Mixed	~20																												
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E26	Definitional Problems with Studies	<p>Epidemiology Definitional Problems with Studies</p> <ul style="list-style-type: none"> • Symptoms are usually multiple and change over time • Various definitions of IBS (Manning, Rome I & II) • Functional diagnosis requires invasive investigations • No population study has investigated subjects, although organic lower-GI pathology is rare <p style="text-align: right;"><small>E26</small></p>																																				
E27	World Prevalence of IBS	<p>Epidemiology World Prevalence of IBS</p> <table border="1"> <thead> <tr> <th>Country/Region</th> <th>Prevalence (%)</th> </tr> </thead> <tbody> <tr> <td>Canada</td> <td>12%</td> </tr> <tr> <td>USA</td> <td>7-10%</td> </tr> <tr> <td>Mexico</td> <td>18%</td> </tr> <tr> <td>Nicaragua</td> <td>13%</td> </tr> <tr> <td>Brazil</td> <td>14%</td> </tr> <tr> <td>Chile</td> <td>28%</td> </tr> <tr> <td>Western Europe</td> <td>3-8%</td> </tr> <tr> <td>Turkey</td> <td>8-10%</td> </tr> <tr> <td>Iran</td> <td>6%</td> </tr> <tr> <td>Israel</td> <td>3-8%</td> </tr> <tr> <td>China</td> <td>6%</td> </tr> <tr> <td>Bangladesh</td> <td>8%</td> </tr> <tr> <td>Singapore</td> <td>8%</td> </tr> <tr> <td>Australia</td> <td>7%</td> </tr> <tr> <td>New Zealand</td> <td>4%</td> </tr> <tr> <td>Japan</td> <td>6-14%</td> </tr> <tr> <td>Taiwan / Hong Kong</td> <td>12-22% / 4-7%</td> </tr> </tbody> </table> <p><small>Predominately Rome II definition</small></p> <p style="text-align: right;"><small>E27</small></p>	Country/Region	Prevalence (%)	Canada	12%	USA	7-10%	Mexico	18%	Nicaragua	13%	Brazil	14%	Chile	28%	Western Europe	3-8%	Turkey	8-10%	Iran	6%	Israel	3-8%	China	6%	Bangladesh	8%	Singapore	8%	Australia	7%	New Zealand	4%	Japan	6-14%	Taiwan / Hong Kong	12-22% / 4-7%
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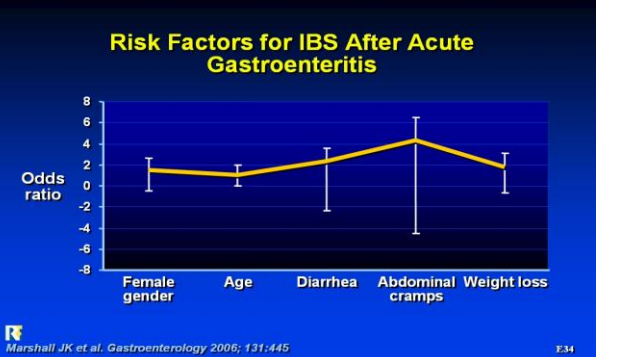
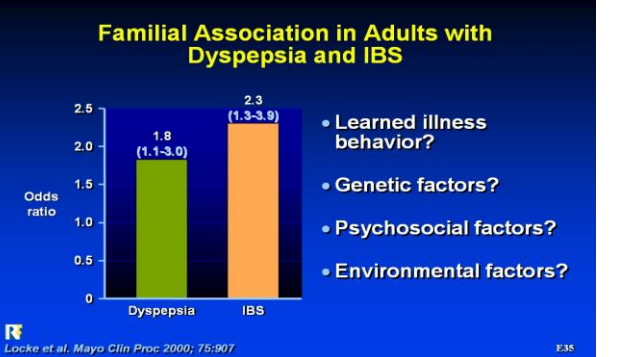
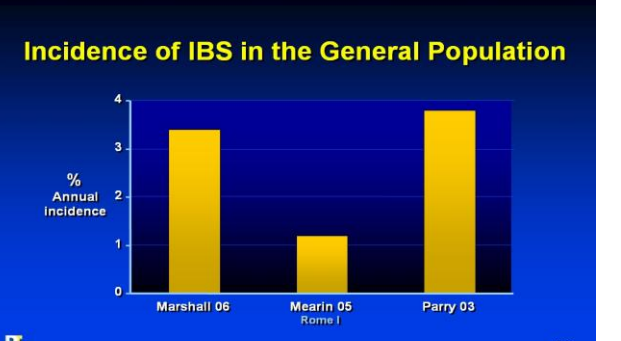
Specialty Modules for Rome Slide Sets Epidemiology

Slide Number	Slide Title	Slide Image																																								
E28	IBS Prevalence According to Sex	 <p>IBS Prevalence According to Sex</p> <table border="1"> <thead> <tr> <th>Study</th> <th>Men (%)</th> <th>Women (%)</th> <th>OR</th> <th>95% CI</th> </tr> </thead> <tbody> <tr> <td>Andrews 2005</td> <td>~5</td> <td>~8</td> <td>0.55</td> <td>(0.5-0.61)</td> </tr> <tr> <td>Thompson 2002</td> <td>~8</td> <td>~15</td> <td>0.52</td> <td>(0.35-0.76)</td> </tr> <tr> <td>Sperber 2005</td> <td>~6</td> <td>~9</td> <td>0.67</td> <td>(0.45-0.99)</td> </tr> <tr> <td>Gwee 2004</td> <td>~8</td> <td>~9</td> <td>0.81</td> <td>(0.60-1.09)</td> </tr> <tr> <td>Talley 2001</td> <td>~4</td> <td>~6</td> <td>0.62</td> <td>(0.3-1.26)</td> </tr> </tbody> </table>	Study	Men (%)	Women (%)	OR	95% CI	Andrews 2005	~5	~8	0.55	(0.5-0.61)	Thompson 2002	~8	~15	0.52	(0.35-0.76)	Sperber 2005	~6	~9	0.67	(0.45-0.99)	Gwee 2004	~8	~9	0.81	(0.60-1.09)	Talley 2001	~4	~6	0.62	(0.3-1.26)										
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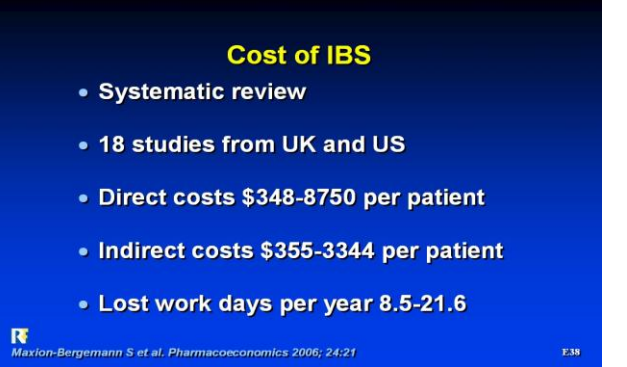
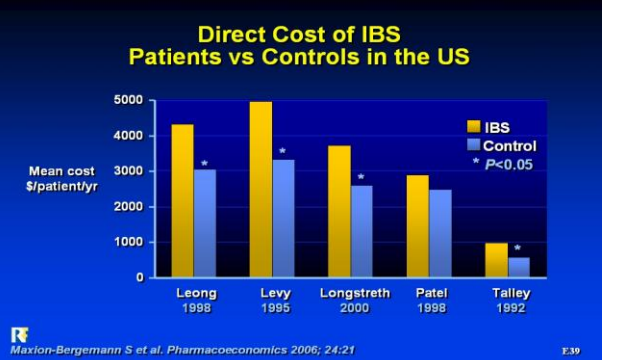
Specialty Modules for Rome Slide Sets Epidemiology

Slide Number	Slide Title	Slide Image																									
E31	IBS Prevalence According to Socioeconomic Status	<p>IBS Prevalence According to Socioeconomic Status</p> <table border="1"> <caption>Approximate data from Slide E31 bar chart</caption> <thead> <tr> <th>Socioeconomic Status</th> <th>Minocha 2006 (US)</th> <th>Wilson 2004 (UK)</th> <th>Andrews 2005 (US)</th> <th>Howell 2004 (New Zealand)</th> </tr> </thead> <tbody> <tr> <td>Very low</td> <td>22</td> <td>13</td> <td>10</td> <td>3</td> </tr> <tr> <td>Low</td> <td>16</td> <td>11</td> <td>8</td> <td>5</td> </tr> <tr> <td>High</td> <td>14</td> <td>12</td> <td>6</td> <td>4</td> </tr> <tr> <td>Very high</td> <td>10</td> <td>11</td> <td>6</td> <td>5</td> </tr> </tbody> </table>	Socioeconomic Status	Minocha 2006 (US)	Wilson 2004 (UK)	Andrews 2005 (US)	Howell 2004 (New Zealand)	Very low	22	13	10	3	Low	16	11	8	5	High	14	12	6	4	Very high	10	11	6	5
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E32	IBS Following Infectious Gastroenteritis	<p>IBS Following Infectious Gastroenteritis</p> <ul style="list-style-type: none"> Systematic review 8 studies 588,061 subjects 3-12 months follow-up 9.8% IBS in cases 1.2% IBS in controls <table border="1"> <caption>Data from Slide E32 forest plot</caption> <thead> <tr> <th>Study</th> <th>Odds Ratio (95% CI)</th> </tr> </thead> <tbody> <tr> <td>Ji 05</td> <td>2.8 (1.0, 7.5)</td> </tr> <tr> <td>Mearin 05</td> <td>8.7 (3.3, 22.6)</td> </tr> <tr> <td>Wang 04</td> <td>10.7 (2.5, 45.6)</td> </tr> <tr> <td>Okhuysen 04</td> <td>10.1 (0.6, 181.4)</td> </tr> <tr> <td>Cumberland 03</td> <td>6.6 (2.0, 22.3)</td> </tr> <tr> <td>Ilnyckij 03</td> <td>2.7 (0.2, 30.2)</td> </tr> <tr> <td>Parry 03</td> <td>9.8 (3.2, 30.0)</td> </tr> <tr> <td>Rodriguez 99</td> <td>11.3 (6.3, 20.1)</td> </tr> <tr> <td>Pooled estimate</td> <td>7.3 (4.8, 11.1)</td> </tr> </tbody> </table> <p>Halvorson HA et al. AJG 2006; 101:1894</p>	Study	Odds Ratio (95% CI)	Ji 05	2.8 (1.0, 7.5)	Mearin 05	8.7 (3.3, 22.6)	Wang 04	10.7 (2.5, 45.6)	Okhuysen 04	10.1 (0.6, 181.4)	Cumberland 03	6.6 (2.0, 22.3)	Ilnyckij 03	2.7 (0.2, 30.2)	Parry 03	9.8 (3.2, 30.0)	Rodriguez 99	11.3 (6.3, 20.1)	Pooled estimate	7.3 (4.8, 11.1)					
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E33	Risk Factors for IBS After Acute Gastroenteritis-Slide 1 of 2	<p>Risk Factors for IBS After Acute Gastroenteritis</p> <ul style="list-style-type: none"> Female gender Younger age Blood in stool Weight loss Abdominal cramps Diarrhea > 7 days <p>Marshall JK et al. Gastroenterology 2006; 131:445</p>																									

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Slide Number	Slide Title	Slide Image
E34	Risk Factors for IBS After Acute Gastroenteritis-Slide 2 of 2	 <p style="text-align: center;">Risk Factors for IBS After Acute Gastroenteritis</p> <p>Marshall JK et al. <i>Gastroenterology</i> 2006; 131:445 E.34</p>
E35	Familial Association in Adults with Dyspepsia and IBS	 <p style="text-align: center;">Familial Association in Adults with Dyspepsia and IBS</p> <ul style="list-style-type: none"> • Learned illness behavior? • Genetic factors? • Psychosocial factors? • Environmental factors? <p>Locke et al. <i>Mayo Clin Proc</i> 2000; 75:907 E.35</p>
E36	Incidence of IBS in the General Population	 <p style="text-align: center;">Incidence of IBS in the General Population</p> <p>Marshall 06, Mearin 05 Rome I, Parry 03 E.36</p>

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Slide Number	Slide Title	Slide Image
E37	Impact of IBS on Quality of Life Compared to the General Population	 <p>Impact of IBS on Quality of Life Compared to the General Population</p> <p>SF-36 score</p> <p>All comparisons $p < 0.001$</p> <p>US general population (n = 2474) IBS (n = 877)</p> <p>Physical function, Role limitations - physical, Bodily pain, Emotional well-being, Vitality, Role limitations - emotional, Social functioning, General health</p> <p><i>Gralnek IM et al., Gastroenterology 2000; 119:654</i></p> <p>E.37</p>
E38	Cost of IBS	 <p>Cost of IBS</p> <ul style="list-style-type: none"> • Systematic review • 18 studies from UK and US • Direct costs \$348-8750 per patient • Indirect costs \$355-3344 per patient • Lost work days per year 8.5-21.6 <p><i>Maxion-Bergemann S et al. Pharmacoeconomics 2006; 24:21</i></p> <p>E.38</p>
E39	Direct Cost of IBS: Patients vs Controls in the US	 <p>Direct Cost of IBS Patients vs Controls in the US</p> <p>Mean cost \$/patient/yr</p> <p>IBS Control * $P < 0.05$</p> <p>Leong 1988, Levy 1995, Longstreth 2000, Patel 1998, Talley 1992</p> <p><i>Maxion-Bergemann S et al. Pharmacoeconomics 2006; 24:21</i></p> <p>E.39</p>

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E40	Direct vs Indirect Costs of IBS	<table border="1"> <caption>Direct vs Indirect Costs of IBS (US\$ per patient)</caption> <thead> <tr> <th>Study</th> <th>Direct Costs (US\$)</th> <th>Indirect Costs (US\$)</th> <th>Total (US\$)</th> </tr> </thead> <tbody> <tr> <td>Akehurst UK</td> <td>565</td> <td>2760</td> <td>3325</td> </tr> <tr> <td>Creed UK</td> <td>1933</td> <td>355</td> <td>2288</td> </tr> <tr> <td>Karampela UK</td> <td>348</td> <td>1028</td> <td>1376</td> </tr> <tr> <td>Karampela US</td> <td>580</td> <td>1300</td> <td>1880</td> </tr> <tr> <td>Leong US</td> <td>4331</td> <td>917</td> <td>5248</td> </tr> </tbody> </table> <p><small>Numbers in bars = IBS costs in US\$ per patient Maxion-Bergemann S et al. Pharmacoeconomics 2006; 24:21</small></p>	Study	Direct Costs (US\$)	Indirect Costs (US\$)	Total (US\$)	Akehurst UK	565	2760	3325	Creed UK	1933	355	2288	Karampela UK	348	1028	1376	Karampela US	580	1300	1880	Leong US	4331	917	5248
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E41	IBS and Surgery	<p>IBS vs non-IBS</p> <ul style="list-style-type: none"> • Cholecystectomy 3-fold higher • Appendectomy 2-fold higher • Hysterectomy 2-fold higher • Back surgery 50% higher <p><small>* Adjusted figures Longstreth FG, Yao JF. Gastroenterology 2004; 126:1665</small></p>																								
E42	US Annual Costs (US\$ Millions)	<table border="1"> <thead> <tr> <th></th> <th>Visits</th> <th>Drugs</th> </tr> </thead> <tbody> <tr> <td>Ulcerative colitis</td> <td>38</td> <td>138</td> </tr> <tr> <td>Foodborne illness</td> <td>155</td> <td>38</td> </tr> <tr> <td>IBS</td> <td>228</td> <td>80</td> </tr> </tbody> </table> <p><small>Sandler RS et al. Gastroenterology 2002; 122:1500</small></p>		Visits	Drugs	Ulcerative colitis	38	138	Foodborne illness	155	38	IBS	228	80												
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Slide Number	Slide Title	Slide Image
E43	World Prevalence of Constipation	<p style="text-align: center;">World Prevalence of Constipation</p> <ul style="list-style-type: none"> • Rome II definition • 15% Canada • 14% Spain • 10% US
E44	Definition of Constipation	<p style="text-align: center;">Definition of Constipation</p> <p>% Constipation</p> <p>Self-report Rome I Rome II</p> <p><i>ParGarrigues V et al. Am J Epidemiol 2004; 159:520</i> <i>Pare P et al. Am J Gastroenterol 2001; 96:3130</i></p>
E45	Constipation and Gender	<p style="text-align: center;">Constipation and Gender</p> <p>% Rome II constipation</p> <p>Women Men</p> <p>Pare 01 Garrigues 04</p> <p>OR = 2.96 (2.06-4.25) OR = 4.58 (1.98-10.6)</p>

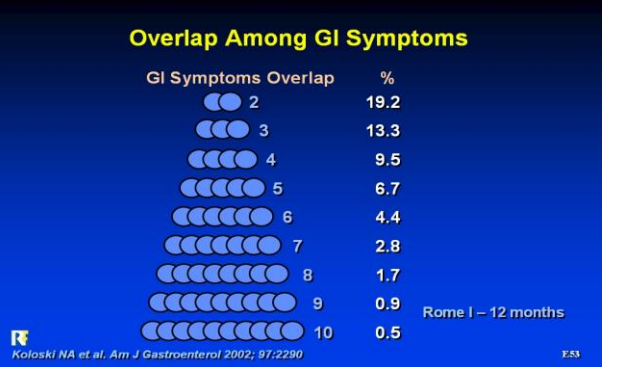


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Slide Number	Slide Title	Slide Image
E46	Constipation and Age	<p>Constipation and Age</p> <p>% Rome II constipation</p> <p>Age</p> <p>Canada Spain US</p> <p><small>Bharucha AE et al. Am J Gastroenterol 2006; 101:604 Pare P et al. Am J Gastroenterol 2001; 96:3130 Garrigues V et al. Am J Epidemiol 2004; 159:520</small></p> <p style="text-align: right;"><small>E46</small></p>
E47	Constipation and Socioeconomic Status	<p>Constipation and Socioeconomic Status</p> <p>% Rome II constipation</p> <p>Annual household income (1000's \$)</p> <p><20 20-40 40-60 60-80 >80</p> <p><small>Pare P et al. AJG 2001; 96:3130</small></p> <p style="text-align: right;"><small>E47</small></p>
E48	Constipation and Quality of life	<p>Constipation and Quality of Life</p> <p>% with one QOL domain moderate/severely reduced</p> <p>No GI symptoms Painless constipation Painful constipation</p> <p><small>Bharucha AE et al. Am J Gastroenterol 2006; 101:604</small></p> <p style="text-align: right;"><small>E48</small></p>


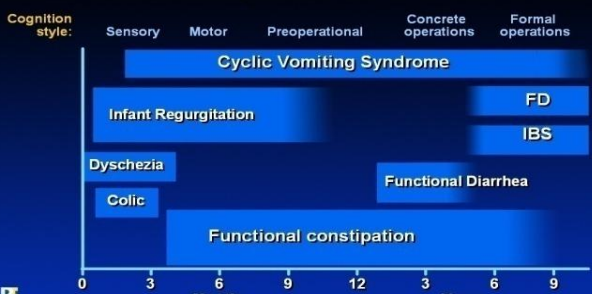


Specialty Modules for Rome Slide Sets Epidemiology

Slide Number	Slide Title	Slide Image																	
E49	Constipation and Exercise: Conflicting Data	<p>Constipation and Exercise: Conflicting Data</p> <p>Exercise score</p> <table border="1"> <thead> <tr> <th>Gender</th> <th>Constipated</th> <th>Not constipated</th> </tr> </thead> <tbody> <tr> <td>Male</td> <td>~2.3</td> <td>~2.3</td> </tr> <tr> <td>Female</td> <td>~2.3</td> <td>~2.3</td> </tr> </tbody> </table> <p>$P=0.79$ (Male), $P=0.57$ (Female)</p> <p>n=723</p> <p>% Constipated</p> <table border="1"> <thead> <tr> <th>Physical exercise</th> <th>% Constipated</th> </tr> </thead> <tbody> <tr> <td>Never</td> <td>~23</td> </tr> <tr> <td>Sometimes</td> <td>~10</td> </tr> <tr> <td>Habitually</td> <td>~7</td> </tr> </tbody> </table> <p>n=349</p> <p>Tuteja AK et al. Am J Gastroenterol 2005; 100:124 Garrigues V et al. Am J Epidemiol 2004; 159:520</p> <p>E49</p>	Gender	Constipated	Not constipated	Male	~2.3	~2.3	Female	~2.3	~2.3	Physical exercise	% Constipated	Never	~23	Sometimes	~10	Habitually	~7
Gender	Constipated	Not constipated																	
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Physical exercise	% Constipated																		
Never	~23																		
Sometimes	~10																		
Habitually	~7																		
E50	Diarrhea in the Population	<p>Diarrhea in the Population</p> <p>Canada = 8.5% (95% CI = 6.9 to 10.1)</p> <p>Australia = 8.1% (95% CI = 7.2 to 9.1)</p> <p>US = 8.1% (95% CI = 5.8 to 10.9)</p> <p>E50</p>																	
E51	Diarrhea and Gender	<p>Diarrhea and Gender</p> <p>% with constipation</p> <table border="1"> <thead> <tr> <th>Study</th> <th>Men</th> <th>Women</th> </tr> </thead> <tbody> <tr> <td>Thompson</td> <td>~9.5</td> <td>~7.0</td> </tr> <tr> <td>Koloski</td> <td>~7.0</td> <td>~8.5</td> </tr> </tbody> </table> <p>Thompson Koloski</p> <p>Boyce PM et al. Intern Med J. 2006; 36:28</p> <p>E51</p>	Study	Men	Women	Thompson	~9.5	~7.0	Koloski	~7.0	~8.5								
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E52	Functional Disorders Overlap	ANAMATION																	



Specialty Modules for Rome Slide Sets Epidemiology

Slide Number	Slide Title	Slide Image																				
E53	Overlap Among GI Symptoms	 <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th>GI Symptoms Overlap</th> <th>%</th> </tr> </thead> <tbody> <tr><td>2</td><td>19.2</td></tr> <tr><td>3</td><td>13.3</td></tr> <tr><td>4</td><td>9.5</td></tr> <tr><td>5</td><td>6.7</td></tr> <tr><td>6</td><td>4.4</td></tr> <tr><td>7</td><td>2.8</td></tr> <tr><td>8</td><td>1.7</td></tr> <tr><td>9</td><td>0.9</td></tr> <tr><td>10</td><td>0.5</td></tr> </tbody> </table> <p style="text-align: right; margin-right: 20px;">Rome I – 12 months</p> <p style="font-size: small; margin-top: 5px;">Koloski NA et al. Am J Gastroenterol 2002; 97:2290 E53</p>	GI Symptoms Overlap	%	2	19.2	3	13.3	4	9.5	5	6.7	6	4.4	7	2.8	8	1.7	9	0.9	10	0.5
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E54	IBS Coexists With Many Other Functional Symptoms	 <p style="text-align: center;">IBS Coexists With Many Other Functional Symptoms</p> <ul style="list-style-type: none"> • Non-GI-specific conditions Fibromyalgia Chronic fatigue syndrome • Non-GI symptoms Headache, back pain, insomnia, gynecology • Psychiatric disorders <p style="font-size: small; margin-top: 5px;">E54</p>																				
E55	IBS - Most Common Diagnosis In Women With Chronic Pelvic Pain	 <p style="text-align: center;">IBS - Most Common Diagnosis In Women With Chronic Pelvic Pain</p> <div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p>General practitioner</p> <p>Nearly 40% of primary care patients with chronic pelvic pain¹</p> </div> <div style="text-align: center;"> <p>Gynecologist</p> <p>Nearly 40% of patients attending a pelvic pain clinic²</p> </div> </div> <p style="font-size: small; margin-top: 5px;">Zondervan KT et al. Am J Obstet Gynecol 2001; 184:1149 Lamvu G et al. Am J Obstet Gynecol 2006; 195:591 E55</p>																				

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Slide Number	Slide Title	Slide Image																								
P1	Pediatrics - Topic Areas	<p>Pediatrics</p> <p>Topic Areas</p> <ul style="list-style-type: none"> • General information, slide 2 • Infant regurgitation, slide 6 • Infant colic, slide 14 • Functional diarrhea, slide 23 • Infant dyschezia, slide 25 • Cyclic vomiting, slide 27 • Abdominal migraine, slide 36 • Rumination syndrome, slide 42 • Functional abdominal pain, IBS and functional dyspepsia, slide 53 • Functional constipation, slide 81 • Non retentive fecal incontinence, slide 102 <p> P1</p>																								
P2	Role of Development in Pediatric FGIDs	<p>Pediatrics</p> <p>Role of Development in Pediatric FGIDs</p>  <p> P2</p>																								
P3	Pediatric FGIDs are Common	<p>Pediatrics</p> <p>Pediatric FGIDs Are Common</p> <table border="1"> <thead> <tr> <th></th> <th>Age</th> <th>%</th> </tr> </thead> <tbody> <tr> <td>Regurgitate at least 4 times/day</td> <td>4 month old infants</td> <td>20</td> </tr> <tr> <td>Colic</td> <td>infants</td> <td>5-19</td> </tr> <tr> <td>Cyclic vomiting</td> <td>school age children</td> <td>2</td> </tr> <tr> <td>Functional dyspepsia</td> <td>school age children</td> <td>5-20</td> </tr> <tr> <td>IBS</td> <td>high school children</td> <td>14</td> </tr> <tr> <td>Abdominal migraine</td> <td>children</td> <td>1-2</td> </tr> <tr> <td>Fecal incontinence</td> <td>school age children</td> <td>1-2</td> </tr> </tbody> </table> <p> P3</p>		Age	%	Regurgitate at least 4 times/day	4 month old infants	20	Colic	infants	5-19	Cyclic vomiting	school age children	2	Functional dyspepsia	school age children	5-20	IBS	high school children	14	Abdominal migraine	children	1-2	Fecal incontinence	school age children	1-2
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P4	Prevalence of Pediatric Constipation	<p>Pediatrics</p> <h3>Prevalence of Pediatric Constipation</h3>  <p>A world map with countries shaded in yellow and orange to represent prevalence rates. The rates are: Canada (5-10%), USA (5-10%), Brazil (10-20%), UK (5-10%), Finland (<5%), Greece (10-15%), Italy (15-20%), Turkey (10-15%), Saudi Arabia (5-10%), Hong Kong (>20%), Japan (10-20%), and Australia (15-20%).</p> <p>van den Berg MM et al. <i>Am J Gastroenterol</i> 2006; 101:2401</p> <p>P4</p>
P5	Prevalence of Functional Abdominal Pain in Children	<p>Pediatrics</p> <h3>Prevalence of Functional Abdominal Pain in Children</h3>  <p>A world map with countries shaded in yellow and orange to represent prevalence rates. The rates are: USA (13%), Italy (10%), United Kingdom (12%), Norway (6%), Sweden (13%), Finland (8%), and Holland (3%).</p> <p>Chitkara DK et al. <i>Am J Gastroenterol</i> 2005; 100:1868</p> <p>P5</p>
P6	Infant Regurgitation: Diagnostic Criteria	<p>Pediatrics</p> <h3>Infant Regurgitation</h3> <p>Diagnostic criteria* Must include all of the following in otherwise healthy infants 3 weeks to 12 months of age:</p> <ul style="list-style-type: none">• Regurgitation two or more times per day for three or more weeks• No retching, hematemesis, aspiration, apnea, failure to thrive, feeding or swallowing difficulties or abnormal posturing <p>P6</p>



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<p>P7</p>	<p>Prevalence of Regurgitation in Healthy Chicago Infants</p>	<p>Pediatrics</p> <p>Prevalence of Regurgitation in Healthy Chicago Infants (n=948)</p> <table border="1"> <caption>Prevalence of Regurgitation in Healthy Chicago Infants (n=948)</caption> <thead> <tr> <th>Age (months)</th> <th>≥ 1 time a day (%)</th> <th>≥ 4 times a day (%)</th> </tr> </thead> <tbody> <tr> <td>0-3</td> <td>~50</td> <td>~15</td> </tr> <tr> <td>4-6</td> <td>~65</td> <td>~25</td> </tr> <tr> <td>7-9</td> <td>~25</td> <td>~5</td> </tr> <tr> <td>10-12</td> <td>~5</td> <td>~2</td> </tr> </tbody> </table> <p>Nelson SP et al. Arch Pediatr Adolesc Med 1997; 151:569</p> <p>P7</p>	Age (months)	≥ 1 time a day (%)	≥ 4 times a day (%)	0-3	~50	~15	4-6	~65	~25	7-9	~25	~5	10-12	~5	~2
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<p>P8</p>	<p>Prevalence of Regurgitation in Healthy Thai Infants</p>	<p>Pediatrics</p> <p>Prevalence of Regurgitation in Healthy Thai Infants (n=216)</p> <table border="1"> <caption>Frequency of regurgitation as a function of age (n = 145)</caption> <thead> <tr> <th>Age (months)</th> <th>% infants presenting with at least 1 regurgitation per day</th> </tr> </thead> <tbody> <tr> <td>2 months</td> <td>~85</td> </tr> <tr> <td>4 months</td> <td>~65</td> </tr> <tr> <td>6 months</td> <td>~45</td> </tr> <tr> <td>8 months</td> <td>~25</td> </tr> <tr> <td>12 months</td> <td>~10</td> </tr> </tbody> </table> <p>Osatakul S et al. J Pediatr Gastroenterol Nutr 2002; 34:63</p> <p>P8</p>	Age (months)	% infants presenting with at least 1 regurgitation per day	2 months	~85	4 months	~65	6 months	~45	8 months	~25	12 months	~10			
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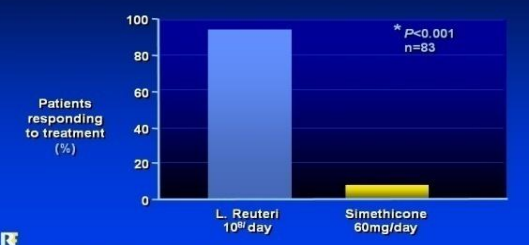
P10	Pathophysiology of Infant Regurgitation	<p>Pediatrics</p> <h3>Pathophysiology of Infant Regurgitation</h3>  <p>The diagram illustrates the pathophysiology of infant regurgitation. On the left, a baby is shown sitting up with a yellow arrow pointing from the stomach up the esophagus, labeled 'Esophagus: short, limited capacity' and 'Poorly accommodating stomach'. On the right, a baby is shown lying down with a yellow arrow pointing from the stomach up the esophagus, labeled 'Gravity + excessive relative volume → regurgitation'. A small 'R' logo is in the bottom left corner, and 'P10' is in the bottom right corner.</p>
P11	Shorter Intra-Abdominal Esophagus in Infants	<p>Pediatrics</p> <h3>Shorter Intra-Abdominal Esophagus in Infants</h3>  <p>The diagram compares the anatomy of the esophagus in an adult and an infant. On the left, an adult's esophagus is shown with a long intra-abdominal segment, labeled 'Adult', 'Lower esophageal sphincter', and 'GEJ'. On the right, an infant's esophagus is shown with a significantly shorter intra-abdominal segment, labeled 'Infant'. Above the infant's diagram, it says 'Adult Increased abdominal pressure'. A small 'R' logo is in the bottom left corner, and 'P11' is in the bottom right corner.</p>
P12	Volume of Feedings: Infant vs Adult	<p>Pediatrics</p> <h3>Volume of Feedings: Infant vs Adult</h3>  <p>The diagram compares the volume of feedings for an infant and an adult. On the left, a silhouette of a 5 kg infant is shown drinking 180 ml from a bottle. On the right, a silhouette of an 80 kg adult is shown drinking 3 liters from a large bottle. Below the silhouettes, it says 'Equivalent amounts consumed in 10 minutes'. A small 'R' logo is in the bottom left corner, and 'P12' is in the bottom right corner.</p>

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P13	Infant Regurgitation Treatment: Commandments	<p>Pediatrics</p> <h3>Commandments for Infant Regurgitation</h3>  <p>The image shows two scrolls on a dark blue background. The left scroll contains the following text: I No seated position, II Do not overfeed. The right scroll contains: III Thickened feedings, IV No smoking.</p> <p>I No seated position</p> <p>II Do not overfeed</p> <p>III Thickened feedings</p> <p>IV No smoking</p> <p>R P13</p>
P14	Infant Colic: Diagnostic Criteria	<p>Pediatrics</p> <h3>Infant Colic</h3> <p>Diagnostic criteria* Must include all of the following in infants from birth to 4 months of age:</p> <ul style="list-style-type: none">• Paroxysms of irritability, fussing or crying that starts and stops without obvious cause• Episodes lasting 3 or more hours/day and occurring at least 3 days/wk for at least 1 week• No failure to thrive <p>R P14</p>
P15	Infant Colic: Theories for Genesis	<p>Pediatrics</p> <h3>Infant Colic</h3> <p>Theories for genesis</p> <ul style="list-style-type: none">• Caretaker/child interaction factors• Difficulty making transitions between sleep and wakefulness• Response to overwhelming sensory stimulation, especially at the end of the day• Abnormal GI motility• Visceral hypersensitivity• Food hypersensitivity  <p>The image shows a close-up of a baby's face, crying with its mouth wide open and eyes closed.</p> <p>R P15</p>

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<p>P16</p>	<p>Differences in Crying Characteristics Between Infants <i>With</i> Colic and Infants <i>Without</i> Colic</p>	<p>Pediatrics Differences in Crying Characteristics Between Infants <i>With</i> Colic and Infants <i>Without</i> Colic</p> <p>Daily Distress: Minutes/day (mean + 1 SD) at 6 weeks and 5 months. Colic group (blue) is significantly higher than No colic group (yellow) at both ages (*P<0.05).</p> <p>Distress Bout Frequency: Bouts/day (mean + 1 SD) at 6 weeks and 5 months. Colic group (blue) is significantly higher than No colic group (yellow) at both ages (*P<0.05).</p> <p>Distress Bout Length: Minutes/bout (mean + 1 SD) at 6 weeks and 5 months. Colic group (blue) is significantly higher than No colic group (yellow) at 6 weeks (*P<0.05), but not significantly different at 5 months (P=n.s.).</p> <p>Legend: Colic (blue), No colic (yellow)</p> <p>Barr RG et al. J Dev Behav Pediatr 2005; 26:14 P16</p>
<p>P17</p>	<p>Reassuring Parents About Infant Crying: The Traffic Light Parable</p>	<p>Pediatrics The Traffic Light Parable</p> <p>Left image: Baby sleeping, green traffic light.</p> <p>Right image: Baby crying, red traffic light.</p> <p>P17</p>
<p>P18</p>	<p>Film: Inconsolable Crying Behavior</p>	<p>P18</p>

<p>P19</p>	<p>Evaluation of Treatment for Infant Colic</p>	<p>Pediatrics</p> <p>Evaluation of Treatment for Infant Colic</p> <table border="1"> <thead> <tr> <th>Treatment</th> <th>Studies evaluated</th> <th>Number of patients</th> <th>Effects</th> </tr> </thead> <tbody> <tr> <td>Simethicone</td> <td>4</td> <td>312</td> <td>-</td> </tr> <tr> <td>Dicyclomine</td> <td>3</td> <td>134</td> <td>+</td> </tr> <tr> <td>Increased carrying and holding baby</td> <td>2</td> <td>94</td> <td>-</td> </tr> <tr> <td>Advice to reduce stimulation</td> <td>1</td> <td>42</td> <td>+/-</td> </tr> <tr> <td>Methyscopolamine</td> <td>1</td> <td>40</td> <td>-</td> </tr> <tr> <td>Training for parents</td> <td>1</td> <td>14</td> <td>-</td> </tr> </tbody> </table> <p>R Garrison MM et al. Pediatrics 2000; 106:184 P19</p>	Treatment	Studies evaluated	Number of patients	Effects	Simethicone	4	312	-	Dicyclomine	3	134	+	Increased carrying and holding baby	2	94	-	Advice to reduce stimulation	1	42	+/-	Methyscopolamine	1	40	-	Training for parents	1	14	-
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<p>P20</p>	<p><i>Lactobacillus reuteri</i> vs Simethicone in the Treatment of Breast-fed Infants with Colic</p>	<p>Pediatrics</p> <p><i>Lactobacillus Reuteri</i> vs Simethicone in the Treatment of Breast-fed Infants with Colic</p>  <p>Patients responding to treatment (%)</p> <p>* $P < 0.001$ n=83</p> <p>L. Reuteri 10⁸/day Simethicone 80mg/day</p> <p>R Savino F et al. Pediatrics 2007; 119:e124 P20</p>																												
<p>P21</p>	<p>Treatment of Infant Colic: Limitations</p>	<p>Pediatrics</p> <p>Treatment of Infant Colic: Limitations</p> <ul style="list-style-type: none"> • Small proportion of studies have been randomized, double-blind and with an appropriate definition of cases • Placebo-treated groups showed reduction of crying in variable proportions: 5% to 85% of infants • Variability may be due to methodological problems or to chance <p>R Garrison MM et al. Pediatrics 2000; 106:184 P21</p>																												

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<p>P22</p>	<p>Severe Infantile Colic May Indicate Susceptibility to GI Disease, Allergy, and Psychological Disorders</p>	<p>Severe Infantile Colic May Indicate Susceptibility to GI Disease, Allergy, and Psychological Disorders</p> <table border="1"> <caption>Approximate data from the bar chart</caption> <thead> <tr> <th>Condition</th> <th>Without colic (%)</th> <th>Colic (%)</th> </tr> </thead> <tbody> <tr> <td>GI disease</td> <td>~1</td> <td>~15</td> </tr> <tr> <td>Recurrent abdominal pain</td> <td>~1</td> <td>~12</td> </tr> <tr> <td>Allergic disease</td> <td>~1</td> <td>~12</td> </tr> <tr> <td>Asthmatic rhinitis-conjunctivitis</td> <td>~1</td> <td>~12</td> </tr> <tr> <td>Psychological disorder</td> <td>~1</td> <td>~18</td> </tr> <tr> <td>Supremacy</td> <td>~1</td> <td>~35</td> </tr> <tr> <td>Fussiness</td> <td>~5</td> <td>~20</td> </tr> <tr> <td>Aggressiveness</td> <td>~2</td> <td>~18</td> </tr> <tr> <td>Enuresis</td> <td>~2</td> <td>~15</td> </tr> <tr> <td>Sleep disorders</td> <td>~5</td> <td>~28</td> </tr> </tbody> </table> <p><small>Savino et al. Acta Paediatrica 2005; 94(Suppl 449):129</small></p>	Condition	Without colic (%)	Colic (%)	GI disease	~1	~15	Recurrent abdominal pain	~1	~12	Allergic disease	~1	~12	Asthmatic rhinitis-conjunctivitis	~1	~12	Psychological disorder	~1	~18	Supremacy	~1	~35	Fussiness	~5	~20	Aggressiveness	~2	~18	Enuresis	~2	~15	Sleep disorders	~5	~28
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<p>P23</p>	<p>Pediatric Functional Diarrhea: Diagnostic Criteria</p>	<p>Pediatrics</p> <p>Functional Diarrhea</p> <p>Diagnostic criteria Must include all of the following:</p> <ul style="list-style-type: none"> • Daily painless, recurrent passage of 3 or more large, unformed stools • Symptoms that last more than 4 weeks • Onset of symptoms that begins between 6 and 36 months of age • Passage of stools that occurs during waking hours • There is no failure-to-thrive if caloric intake is adequate 																																	
<p>P24</p>	<p>Pediatric Functional Diarrhea: Possible Contributory Factors</p>	<p>Pediatrics</p> <p>Functional Diarrhea Possible Contributory Factors</p> <pre> graph TD A[Disordered small-intestinal motility] --> D[Diarrhea] B[Dietary fat restriction] --> D C[Fructose and/or sorbitol malabsorption] --> D E[Bile salts malabsorption] --> D </pre>																																	

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P25	Infant Dyschezia: Diagnostic Criteria	<p>Pediatrics</p> <h3>Infant Dyschezia</h3> <p>Diagnostic criteria Must include in an infant less than 6 months of age:</p> <ul style="list-style-type: none">• At least 10 minutes of straining and crying before successful passage of soft stools, <p>and</p> <ul style="list-style-type: none">• No other health problems <p> Hyman PE et al. Gastroenterology 2006; 130:1519 P25</p>
P26	Infant Dyschezia: Treatment	<p>Pediatrics</p> <h3>Infant Dyschezia</h3>  <p>Treatment</p> <ul style="list-style-type: none">• Perform thorough physical exam• Avoid repeated anal stimulation• Provide reassurance that this is a transient condition for which no further treatment or testing is needed• Assure continuing availability <p> P26</p>
P27	Pediatric Cyclic Vomiting: Diagnostic Criteria	<p>Pediatrics</p> <h3>Cyclic Vomiting</h3> <p>Diagnosis: Must include all of the following:</p> <ul style="list-style-type: none">• Two or more episodes of intense nausea and unremitting vomiting or retching lasting hours to days• Return to usual state of health lasting weeks to months <p> P27</p>

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<p>P28</p>	<p>Cyclic vs Chronic Vomiting in Children</p>	<p>Pediatrics</p> <h3>Cyclic vs Chronic Vomiting</h3> <p># Episodes of vomiting</p> <p>Days</p> <p>— Cyclic — Chronic</p> <p><small>Pfau BT et al. Pediatrics 1996; 97:364</small></p> <p><small>P28</small></p>
<p>P29</p>	<p>Pediatric CVS: On-Off, Intense, Stereotypical-Slide 1 of 2</p>	<p>Pediatrics</p> <h3>CVS: On-off, Intense, Stereotypical</h3> <p>Vomiting: 6X/hr</p> <p>Episode: lethargy, pallor, anorexia, nausea, pain, retching (> 77%)</p> <p>Well</p> <p>24-41 hrs</p> <p>Prodrome (30 min): lethargy, pallor, anorexia, nausea</p> <p>Recovery (5 hrs)</p> <p><small>LI BU et al. Adv Pediatr 2000; 47:117</small></p> <p><small>P29</small></p>
<p>P30</p>	<p>Pediatric CVS: On-Off, Intense, Stereotypical-Slide 2 of 2</p>	<p>Pediatrics</p> <h3>CVS: On-Off, Intense, Stereotypical</h3> <p>Nausea</p> <p>24-43 hrs</p> <p>Well</p> <p>Recovery</p> <p><small>LI BU et al. Adv Pediatr 2000;47:117</small></p> <p><small>P30</small></p>

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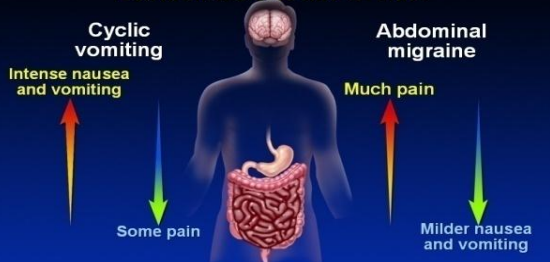
<p>P31</p>	<p>Characteristics of Pediatric Cyclic Vomiting Syndrome</p>	<p>Pediatrics</p> <p>Characteristics of Cyclic Vomiting Syndrome</p> <table border="1"> <thead> <tr> <th>Characteristic</th> <th>Percentage (%)</th> </tr> </thead> <tbody> <tr> <td>Recurrent episodes</td> <td>100</td> </tr> <tr> <td>Asymptomatic between episodes</td> <td>100</td> </tr> <tr> <td>Stereotypical episodes</td> <td>100</td> </tr> <tr> <td>Pallor and lethargy</td> <td>~90</td> </tr> <tr> <td>Family history of migraine</td> <td>~85</td> </tr> <tr> <td>Intense vomiting (> 4 emeses/hr)</td> <td>~75</td> </tr> </tbody> </table> <p><small>LI BU et al. Adv Pediatr 2000; 47:117</small></p> <p>P31</p>	Characteristic	Percentage (%)	Recurrent episodes	100	Asymptomatic between episodes	100	Stereotypical episodes	100	Pallor and lethargy	~90	Family history of migraine	~85	Intense vomiting (> 4 emeses/hr)	~75																						
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<p>P32</p>	<p>Symptoms Associated with Pediatric CVS</p>	<p>Pediatrics</p> <p>Associated Symptoms with CVS</p> <table border="1"> <thead> <tr> <th>Symptom</th> <th>Percentage (%)</th> <th>Category</th> </tr> </thead> <tbody> <tr> <td>Lethargy</td> <td>~90</td> <td>Systemic symptoms</td> </tr> <tr> <td>Pallor</td> <td>~85</td> <td>Systemic symptoms</td> </tr> <tr> <td>Withdrawal</td> <td>~40</td> <td>Systemic symptoms</td> </tr> <tr> <td>Flushing</td> <td>~25</td> <td>Systemic symptoms</td> </tr> <tr> <td>Salivation</td> <td>~20</td> <td>Systemic symptoms</td> </tr> <tr> <td>Fever</td> <td>~15</td> <td>Systemic symptoms</td> </tr> <tr> <td>Headaches</td> <td>~40</td> <td>Neurological symptoms</td> </tr> <tr> <td>Photophobia</td> <td>~35</td> <td>Neurological symptoms</td> </tr> <tr> <td>Phonophobia</td> <td>~25</td> <td>Neurological symptoms</td> </tr> <tr> <td>Vertigo</td> <td>~20</td> <td>Neurological symptoms</td> </tr> <tr> <td>Seizures</td> <td>~5</td> <td>Neurological symptoms</td> </tr> </tbody> </table> <p><small>LI BU et al. Dig Dis Sci 1999; 44(Suppl):13</small></p> <p>P32</p>	Symptom	Percentage (%)	Category	Lethargy	~90	Systemic symptoms	Pallor	~85	Systemic symptoms	Withdrawal	~40	Systemic symptoms	Flushing	~25	Systemic symptoms	Salivation	~20	Systemic symptoms	Fever	~15	Systemic symptoms	Headaches	~40	Neurological symptoms	Photophobia	~35	Neurological symptoms	Phonophobia	~25	Neurological symptoms	Vertigo	~20	Neurological symptoms	Seizures	~5	Neurological symptoms
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<p>P33</p>	<p>Pediatric Cyclic Vomiting Syndrome: Episode Triggers</p>	<p>Pediatrics</p> <p>Episode Triggers</p> <table border="1"> <thead> <tr> <th>Trigger</th> <th>Percentage (%)</th> </tr> </thead> <tbody> <tr> <td>Psychosocial</td> <td>40</td> </tr> <tr> <td>None</td> <td>20-30</td> </tr> <tr> <td>Infectious</td> <td>29</td> </tr> <tr> <td>Exhaustion</td> <td>20</td> </tr> <tr> <td>Atopic</td> <td>9</td> </tr> <tr> <td>Dietary</td> <td>24</td> </tr> <tr> <td>Menses</td> <td>15</td> </tr> <tr> <td>Motion</td> <td>10</td> </tr> </tbody> </table> <p><small>LI BU et al. Dig Dis Sci 1999; 44(Suppl):13</small></p> <p>P33</p>	Trigger	Percentage (%)	Psychosocial	40	None	20-30	Infectious	29	Exhaustion	20	Atopic	9	Dietary	24	Menses	15	Motion	10																		
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<p>P34</p>	<p>Pediatric Cyclic Vomiting Syndrome: Diagnostic Considerations</p>	<p>Pediatrics</p> <p>Metabolic</p> <ul style="list-style-type: none"> • During the episode <ul style="list-style-type: none"> • Blood: electrolytes, glucose, NH₄, lactate, amino acids, SGPT, GGTP, amylase, lipase • Urine: UA, organic acids, 8-ALA & porphobilinogen <p>Radiology</p> <ul style="list-style-type: none"> • UGI with SBFT, abdominal U/S, head MRI <p>Miscellaneous</p> <ul style="list-style-type: none"> • EEG, pregnancy test, toxicology <p>Endoscopic</p> <ul style="list-style-type: none"> • EGD + biopsies <p>Diagnostic Considerations</p> <p>R</p> <p>P34</p>
<p>P35</p>	<p>Management of Pediatric Cyclic Vomiting Syndrome</p>	<p>Pediatrics</p> <p>Management of Cyclic Vomiting Syndrome</p> <ul style="list-style-type: none"> • Prophylaxis: Indicated for frequent bouts, (e.g., monthly) <ul style="list-style-type: none"> cyproheptadine amitriptyline propranolol • Abortive care: antimigraine agents • Acute episodes – supportive care <ul style="list-style-type: none"> Hydration – intravenous Anti-emetics – ondansetron Sedation – lorazepam Hemorrhage – prevent with PPI <p>R</p> <p>P35</p>
<p>P36</p>	<p>Progression: CVS to Abdominal Migraine to Migraine Headache</p>	<p>Pediatrics</p> <p>Progression: CVS to Abdominal Migraine to Migraine Headache</p> <p>R</p> <p>P36</p>

<p>P37</p>	<p>Abdominal Migraine: Diagnostic Criteria</p>	<p>Pediatrics</p> <h3>Abdominal Migraine</h3> <p>Diagnostic criteria* Must include all of the following:</p> <ul style="list-style-type: none"> • Paroxysmal episodes of intense, acute periumbilical pain that lasts for 1 hour or more • Intervening periods of usual health lasting weeks to months • The pain interferes with normal activities • The pain is associated with at least 2 of the following: <ul style="list-style-type: none"> ◦ Anorexia ◦ Nausea ◦ Vomiting ◦ Headache ◦ Photophobia ◦ Pallor • No evidence of an inflammatory, anatomic, metabolic or neoplastic process considered that explains the subject's symptoms <p>* Criteria fulfilled two or more times in the preceding 12 months</p> <p>R</p> <p>P37</p>																											
<p>P38</p>	<p>Abdominal Migraine is a Real Entity</p>	<p>Pediatrics</p> <p>Abdominal Migraine is a Real Entity</p> <p>R</p> <p>Russell G et al. <i>Pediatr Drugs</i> 2002; 4:1</p> <p>P38</p>																											
<p>P39</p>	<p>Similar Features in Abdominal Migraine and Migraine Headaches</p>	<p>Pediatrics</p> <h3>Similar Features in Abdominal Migraine and Migraine Headaches</h3> <table border="1"> <thead> <tr> <th>Feature</th> <th>Abdominal Migraine %</th> <th>Migraine Headache %</th> </tr> </thead> <tbody> <tr> <td>Nausea</td> <td>100</td> <td>80</td> </tr> <tr> <td>Pallor</td> <td>90</td> <td>90</td> </tr> <tr> <td>Vomiting</td> <td>50</td> <td>55</td> </tr> <tr> <td>Motion sickness</td> <td>50</td> <td>50</td> </tr> <tr> <td>Migraine in mother</td> <td>50</td> <td>40</td> </tr> <tr> <td>Visual disturbances</td> <td>20</td> <td>40</td> </tr> <tr> <td>Vertigo/dizziness</td> <td>20</td> <td>30</td> </tr> <tr> <td>Migraine in father</td> <td>18</td> <td>22</td> </tr> </tbody> </table> <p>R</p> <p>Russell G et al. <i>Pediatr Drugs</i> 2002; 4:1</p> <p>P39</p>	Feature	Abdominal Migraine %	Migraine Headache %	Nausea	100	80	Pallor	90	90	Vomiting	50	55	Motion sickness	50	50	Migraine in mother	50	40	Visual disturbances	20	40	Vertigo/dizziness	20	30	Migraine in father	18	22
Feature	Abdominal Migraine %	Migraine Headache %																											
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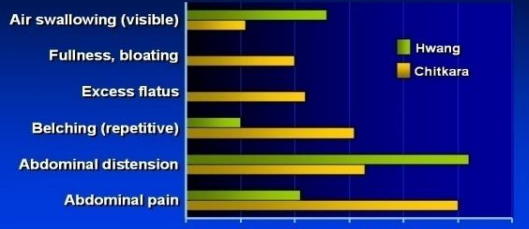

<p>P40</p>	<p>Treatment and Prognosis of Abdominal Migraine</p>	<p>Pediatrics</p> <p>Treatment and Prognosis of Abdominal Migraine</p> <ul style="list-style-type: none"> • Treatment- Determined by the frequency and severity of attacks <ol style="list-style-type: none"> 1. Explanation and reassurance 2. Avoid triggers (stress, travel, fasting, lack of sleep) 3. Medication: pizotifen, cyproheptadine, amitriptyline, propranolol • Prognosis Most resolve, although many develop migraine headaches <p>R</p> <p>P40</p>
<p>P41</p>	<p>Paroxysmal Disorders Involving Interactions Between the CNS and GI Tract</p>	<p>Pediatrics</p> <p>Paroxysmal Disorders Involving Interactions Between the CNS and GI Tract</p>  <p>R</p> <p>P41</p>
<p>P42</p>	<p>Infant Rumination Syndrome: Diagnostic Criteria</p>	<p>Pediatrics</p> <p>Infant Rumination Syndrome</p> <p>Diagnostic criteria* Must include all of the following for at least 3 months:</p> <ul style="list-style-type: none"> • Repetitive contractions of the abdominal muscles, diaphragm, and tongue • Regurgitation of gastric content into the mouth, which is either expectorated or rechewed and reswallowed • Three or more of the following: <ul style="list-style-type: none"> - Onset between 3 and 8 months - Does not respond to management for gastro-esophageal reflux disease, or to anticholinergic drugs, hand restraints, formula changes, and gavage or gastrostomy feedings - Unaccompanied by signs of nausea or distress - Does not occur during sleep and when the infant is interacting with individuals in the environment <p>R</p> <p>Hyman PE et al. Gastroenterology 2006; 130:1519</p> <p>P42</p>

<p>P43</p>	<p>Risk Factors for Infant Rumination</p>	<p>Pediatrics</p> <p>Risk Factors for Infant Rumination</p> <p>Infant rumination</p> <p>P43</p>
<p>P44</p>	<p>Adolescent Rumination Syndrome: Diagnostic Criteria</p>	<p>Pediatrics</p> <p>Adolescent Rumination Syndrome</p> <p>Diagnostic criteria* Must include all of the following:</p> <ul style="list-style-type: none"> • Repeated painless regurgitation and re-chewing or expulsion of food that: <ul style="list-style-type: none"> • begins soon after ingestion of a meal • does not occur during sleep • does not respond to standard treatment for GER • No retching • No evidence of an inflammatory, anatomic, metabolic or neoplastic process that explains the subject's symptoms <p>* Criteria fulfilled at least once per week for at least 2 months prior to diagnosis</p> <p>P44</p>
<p>P45</p>	<p>Adolescent Rumination Syndrome: Study Data</p>	<p>Pediatrics</p> <p>Adolescent Rumination Syndrome</p> <ul style="list-style-type: none"> • 147 children (68% females) • Age at diagnosis: 15.0 ± 0.3 years • Duration of symptoms: 2.2 years • 73% missed school/work • 46% hospitalized for symptoms • 11% surgery <p>P45</p>

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<p>P46</p>	<p>Esophagogastric Manometry in the Rumination Syndrome</p>	<p>Pediatrics</p> <h3>Rumination Syndrome</h3> <p>Pharynx UES Esophagus 1 Esophagus 2 Esophagus 3 Esophagus 4 LES Stomach</p> <p>Swallow Strain + rumination</p> <p>R P46</p>
<p>P47</p>	<p>Antroduodenal Manometry and pH Monitoring of the Distal Esophagus in the Rumination Syndrome</p>	<p>Pediatrics</p> <h3>Rumination Syndrome</h3> <p>pH probe Antroduodenal 1 2 3 4 5 Desc duodenal Distal duodenal Proximal jejunal Regurgitation</p> <p>7 5.5 4 30 0 mmHg</p> <p>4 minutes</p> <p><i>O'Brien et al Gastroenterology 1995; 108:1024</i></p> <p>R P47</p>
<p>P48</p>	<p>Adolescent Rumination Syndrome: Treatment Options</p>	<p>Pediatrics</p> <h3>Treatment Options</h3> <p>Adolescent rumination syndrome</p> <ul style="list-style-type: none"> Reassurance and education Behavioral techniques Diaphragmatic breathing Hypnotherapy NO donors? HT1 agonists? NJ feeds Anti-depressants Biofeedback <p>R P48</p>

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<p>P49</p>	<p>Differential Diagnosis of Rumination</p>	<p>Pediatrics</p> <h3>Differential Diagnosis of Rumination</h3> <table border="1"> <thead> <tr> <th></th> <th>Vomiting</th> <th>Esophagitis</th> <th>Prokinetics</th> <th>Fundoplication</th> </tr> </thead> <tbody> <tr> <td>GERD</td> <td>Frequent regurgitation</td> <td>Often</td> <td>Helpful</td> <td>Helpful</td> </tr> <tr> <td>Gastroparesis</td> <td>Hours after meal</td> <td>No</td> <td>Helpful</td> <td>Not helpful</td> </tr> <tr> <td>Cyclic Vomiting</td> <td>Intermittent, not meal-related</td> <td>During episodes</td> <td>Not helpful</td> <td>Not helpful</td> </tr> <tr> <td>Rumination</td> <td>During or minutes after meal</td> <td>No</td> <td>Not helpful</td> <td>Not helpful</td> </tr> </tbody> </table> <p> P 49</p>		Vomiting	Esophagitis	Prokinetics	Fundoplication	GERD	Frequent regurgitation	Often	Helpful	Helpful	Gastroparesis	Hours after meal	No	Helpful	Not helpful	Cyclic Vomiting	Intermittent, not meal-related	During episodes	Not helpful	Not helpful	Rumination	During or minutes after meal	No	Not helpful	Not helpful
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<p>P50</p>	<p>Aerophagia: Diagnostic Criteria</p>	<p>Pediatrics</p> <h3>Aerophagia</h3> <p>Diagnostic criteria*</p> <p>Must include at least two of the following:</p> <ul style="list-style-type: none"> • Air swallowing • Abdominal distension due to intraluminal air • Repetitive belching and/or increased flatus <p>* Criteria fulfilled at least once per week for at least two months prior to diagnosis</p> <p> P 50</p>																									
<p>P51</p>	<p>Clinical Manifestations in Children with Aerophagia</p>	<p>Pediatrics</p> <h3>Clinical Manifestations in Children with Aerophagia</h3>  <table border="1"> <caption>Clinical Manifestations in Children with Aerophagia</caption> <thead> <tr> <th>Manifestation</th> <th>Hwang (%)</th> <th>Chitkara (%)</th> </tr> </thead> <tbody> <tr> <td>Air swallowing (visible)</td> <td>~25</td> <td>~10</td> </tr> <tr> <td>Fullness, bloating</td> <td>~15</td> <td>~18</td> </tr> <tr> <td>Excess flatus</td> <td>~15</td> <td>~20</td> </tr> <tr> <td>Belching (repetitive)</td> <td>~10</td> <td>~30</td> </tr> <tr> <td>Abdominal distension</td> <td>~50</td> <td>~35</td> </tr> <tr> <td>Abdominal pain</td> <td>~20</td> <td>~50</td> </tr> </tbody> </table> <p> <small>Hwang JB et al. J Pediatr Gastroenterol Nutr 2005; 41:612 Chitkara DS et al. Neurogastroenterol Motil 2005; 4:518</small> P 51</p>	Manifestation	Hwang (%)	Chitkara (%)	Air swallowing (visible)	~25	~10	Fullness, bloating	~15	~18	Excess flatus	~15	~20	Belching (repetitive)	~10	~30	Abdominal distension	~50	~35	Abdominal pain	~20	~50				
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<p>P52</p>	<p>Esophageal Air Sign in Patients with Aerophagia and in Controls</p>	<p>Pediatrics</p> <p>Esophageal Air Sign in Patients with Aerophagia and in Controls</p>  <p>Hwang JB et al, J Pediatr Gastroenterol Nutr 2005; 41:612</p> <p>P52</p>		
<p>P53</p>	<p>Recurrent Abdominal Pain (RAP) vs Functional Gastrointestinal Disorder (FGID)</p>	<p>Pediatrics</p> <p>Recurrent Abdominal Pain (RAP) vs Functional Gastrointestinal Disorder (FGID)</p> <table border="1" data-bbox="1381 641 1837 844"> <tr> <td> <p>RAP</p> <p>Description: rule out disease</p> <p>Lumping</p> <p>Medical model</p> </td> <td> <p>FGID</p> <p>Symptom-based diagnosis</p> <p>Splitting</p> <p>Biopsychosocial model</p> </td> </tr> </table> <p>R</p> <p>P53</p>	<p>RAP</p> <p>Description: rule out disease</p> <p>Lumping</p> <p>Medical model</p>	<p>FGID</p> <p>Symptom-based diagnosis</p> <p>Splitting</p> <p>Biopsychosocial model</p>
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<p>P54</p>	<p>Irritable Bowel Syndrome in Children and Adolescents: Diagnostic Criteria</p>	<p>Pediatrics</p> <p>Irritable Bowel Syndrome</p> <p>Diagnostic criteria* Must include all of the following:</p> <p>Abdominal discomfort** or pain associated with two or more at least 25% of the time:</p> <ul style="list-style-type: none"> • Improved with defecation • Onset associated with a change in frequency of stool • Onset associated with a change in form (appearance) of stool • No evidence of an inflammatory, anatomic, metabolic or neoplastic process that explains the subject's symptoms <p>* Criteria fulfilled at least once per week for at least two months prior to diagnosis ** Discomfort* means an uncomfortable sensation not described as pain</p> <p>R</p> <p>P54</p>		

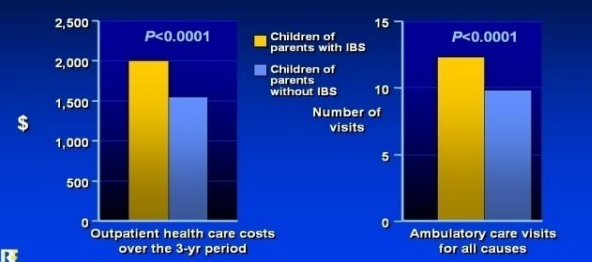
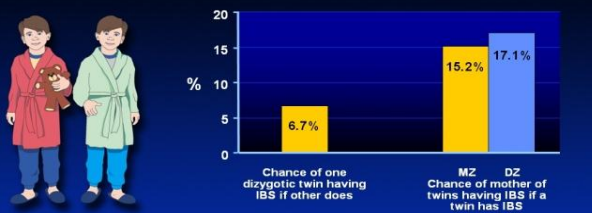
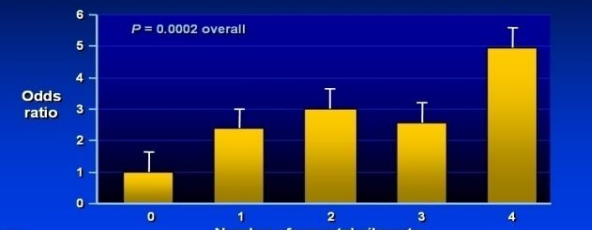
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<p>P55</p>	<p>Pediatric Functional Abdominal Pain: Diagnostic Criteria</p>	<p>Pediatrics</p> <p>Functional Abdominal Pain</p> <p>Diagnostic criteria* Must include all of the following:</p> <ul style="list-style-type: none"> • Episodic or continuous abdominal pain • Insufficient criteria for other FGIDs • No evidence of an inflammatory, anatomic, metabolic or neoplastic process that explains the subject's symptoms <p>* Criteria fulfilled at least once per week for at least 2 months prior to diagnosis</p> <p>R</p> <p>P55</p>												
<p>P56</p>	<p>Abdominal Pain and IBS: Prevalence in Adolescents</p>	<p>Pediatrics</p> <p>Abdominal Pain and IBS: Prevalence</p> <table border="1"> <caption>Abdominal Pain and IBS: Prevalence</caption> <thead> <tr> <th>Age Group</th> <th>RAP (%)</th> <th>IBS (%)</th> </tr> </thead> <tbody> <tr> <td>Middle school</td> <td>~13</td> <td>~7</td> </tr> <tr> <td>High school</td> <td>~17</td> <td>~14</td> </tr> <tr> <td>Adults</td> <td>0</td> <td>~21</td> </tr> </tbody> </table> <p>R</p> <p>Hyams JS et al. J Pediatr 1996; 129:220</p> <p>P56</p>	Age Group	RAP (%)	IBS (%)	Middle school	~13	~7	High school	~17	~14	Adults	0	~21
Age Group	RAP (%)	IBS (%)												
Middle school	~13	~7												
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<p>P57</p>	<p>Lower QOL in Children with Functional Abdominal Pain</p>	<p>Pediatrics</p> <p>Lower QOL in Children with Functional Abdominal Pain</p> <table border="1"> <caption>Lower QOL in Children with Functional Abdominal Pain</caption> <thead> <tr> <th>Group</th> <th>Quality of Life Score (0-100)</th> </tr> </thead> <tbody> <tr> <td>HC (Children self reported QOL)</td> <td>~88</td> </tr> <tr> <td>IBD (Children self reported QOL)</td> <td>~84</td> </tr> <tr> <td>FAP (Children self reported QOL)</td> <td>~78</td> </tr> <tr> <td>Report of parents of children with FAP</td> <td>~70</td> </tr> </tbody> </table> <p>* P<0.05 vs healthy controls and vs parents</p> <p>R</p> <p>Youssef NN et al. Pediatrics 2006; 117:54</p> <p>P57</p>	Group	Quality of Life Score (0-100)	HC (Children self reported QOL)	~88	IBD (Children self reported QOL)	~84	FAP (Children self reported QOL)	~78	Report of parents of children with FAP	~70		
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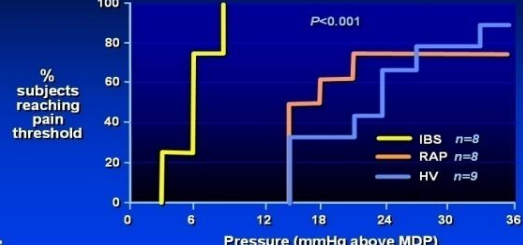
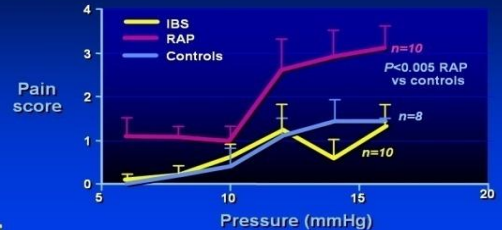
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<p>P58</p>	<p>Pain-Predominant FGID-Pediatric</p>	<p>Pediatrics</p> <h3>Pain-Predominant FGID</h3> <p>Sensitizing medical events: Inflammation (infection, allergies) Distension Trauma Stress Motility disorder</p> <p>Genetic predisposition → Visceral hyperalgesia → Disability</p> <p>Early life events</p> <p>Sensitizing psychosocial events: Depression Anxiety Family stress Coping style Secondary gains</p> <p><small>R</small></p> <p><small>P58</small></p>												
<p>P59</p>	<p>Biopsychosocial Model of Pain & Coping in Children</p>	<p>Pediatrics</p> <h3>Biopsychosocial Model</h3> <p><small>R</small></p> <p><small>Walker LS et al. Health Psychol 2005; 24:364</small></p> <p><small>P59</small></p>												
<p>P60</p>	<p>Do Noxious Early Life Events Predispose to FGID?</p>	<p>Pediatrics</p> <h3>Do Noxious Early Life Events Predispose to FGID?</h3> <table border="1"> <thead> <tr> <th>Event Category</th> <th>Controls (siblings) (%)</th> <th>Cases (hospitalized for FGID) (%)</th> </tr> </thead> <tbody> <tr> <td>Gastric suction</td> <td>~11</td> <td>~21</td> </tr> <tr> <td>Trauma score > 0</td> <td>~26</td> <td>~29</td> </tr> <tr> <td>Asphyxia score > 0</td> <td>~33</td> <td>~27</td> </tr> </tbody> </table> <p>Odds ratio: 2.99; P<0.009</p> <p><small>R</small></p> <p><small>Anand KJ et al. J Pediatr 2004; 144:449</small></p> <p><small>P60</small></p>	Event Category	Controls (siblings) (%)	Cases (hospitalized for FGID) (%)	Gastric suction	~11	~21	Trauma score > 0	~26	~29	Asphyxia score > 0	~33	~27
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<p>P61</p>	<p>Health Care Cost and Use Over a 3-year Calendar Period for All Children of IBS Parents</p>	<p>Pediatrics</p> <p>Health Care Cost and Use Over a 3-yr Calendar Period for All Children of IBS Parents</p>  <p>Legend: Children of parents with IBS (Yellow), Children of parents without IBS (Blue)</p> <p>Outpatient health care costs over the 3-yr period: $P < 0.0001$</p> <p>Ambulatory care visits for all causes: $P < 0.0001$</p> <p>Levy RL et al. <i>Am J Gastroenterol</i> 2000; 95:451</p> <p>P61</p>
<p>P62</p>	<p>Evidence for Social Learning over Genetics in Twin Study</p>	<p>Evidence for Social Learning over Genetics in Twin Study</p>  <p>Chance of one dizygotic twin having IBS if other does: 6.7%</p> <p>MZ: 15.2%</p> <p>DZ: 17.1%</p> <p>Levy RL et al. <i>Gastroenterology</i> 2001;121:799</p> <p>P62</p>
<p>P63</p>	<p>Relation Between Childhood Functional Abdominal Pain and Parental Health Complaints</p>	<p>Pediatrics</p> <p>Relation Between Childhood Functional Abdominal Pain and Parental Health Complaints</p>  <p>$P = 0.0002$ overall</p> <p>Odds ratio</p> <p>Number of parental ailments</p> <p>Hotopf M et al. <i>BMJ</i> 1998; 316:1196</p> <p>P63</p>

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<p>P64</p>	<p>Barostat Function</p>	<p>Pediatrics</p> <p>Barostat Function</p>  <p>P64</p>
<p>P65</p>	<p>Rectal Barostat Demonstrates Visceral Hyperalgesia in Children</p>	<p>Pediatrics</p> <p>Rectal Barostat Demonstrates Visceral Hyperalgesia</p>  <p>Van Ginkel R et al. <i>Gastroenterology</i> 2001; 120:31</p> <p>P65</p>
<p>P66</p>	<p>Gastric Barostat Demonstrates Visceral Hyperalgesia in Children</p>	<p>Pediatrics</p> <p>Gastric Barostat Demonstrates Visceral Hyperalgesia</p>  <p>Di Lorenzo C et al. <i>J Pediatr</i> 2001; 139:838</p> <p>P66</p>


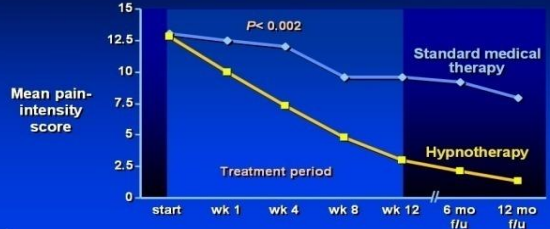
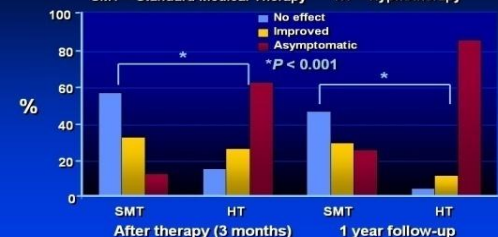
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Pediatric

<p>P67</p>	<p>Reproducibility of Pain During Rectal Barostat Testing in Children</p>	<p>Pediatrics</p> <p>Reproducibility of Pain During Rectal Barostat Testing</p>  <table border="1"> <thead> <tr> <th>Correlation pain localization</th> <th>%</th> </tr> </thead> <tbody> <tr> <td>IBS</td> <td>90%</td> </tr> <tr> <td>Functional abdominal pain</td> <td>87%</td> </tr> <tr> <td>Functional dyspepsia</td> <td>17%</td> </tr> </tbody> </table> <p>R Faure C et al. J Pediatr 2007; 150:66</p> <p>P67</p>	Correlation pain localization	%	IBS	90%	Functional abdominal pain	87%	Functional dyspepsia	17%
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<p>P68</p>	<p>Parent Attention vs Distraction-Pediatric</p>	<p>Pediatrics</p> <p>Parent Attention vs. Distraction</p> <p>Questionnaire-Reported GI Symptom Ratings (range 0-20)</p>  <ul style="list-style-type: none"> • Pain induced by water-load test • Parents randomized to using distraction or attention in their interaction with children in pain • All mothers felt distraction was inappropriate response to pain <p>R Walker LS et al. Pain 2006, 122:43</p> <p>P68</p>								
<p>P69</p>	<p>Mother's/Child's Agenda-Pediatric</p>	<p>Pediatrics</p> <p>Mother's / Child's Agenda</p>  <p>R</p> <p>P69</p>								

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<p>P70</p>	<p>Doctor's Incorrect Agenda-Pediatric</p>	<p>Pediatrics Doctor's Incorrect Agenda</p> <p>Not another one, please These people are crazy! How can I get rid of them? Could it be porphyria? It does not look like she is in pain This is going to take too long Should I treat her for <i>H pylori</i>?</p> <p>P70</p>																								
<p>P71</p>	<p>Doctor's Correct Agenda-Pediatric</p>	<p>Pediatrics Doctor's Correct Agenda</p> <p>Another challenging case It is tough for the family How can I help them? This is clearly an FGID I know the pain is real I cannot rush this Is this patient a candidate for a TCA?</p> <p>P71</p>																								
<p>P72</p>	<p>Adult Outcomes of Functional Abdominal Pain</p>	<p>Pediatrics Adult Outcomes of Functional Abdominal Pain</p> <table border="1"> <thead> <tr> <th>Category</th> <th>Control (Blue)</th> <th>Abdominal pain (Yellow)</th> <th>P-value</th> </tr> </thead> <tbody> <tr> <td>Somatization</td> <td>~3.5</td> <td>~5.5</td> <td>$P < 0.06$</td> </tr> <tr> <td>Global severity</td> <td>~1.0</td> <td>~1.5</td> <td>$P < 0.006$</td> </tr> <tr> <td>Phobic activity</td> <td>~1.0</td> <td>~2.0</td> <td>$P < 0.001$</td> </tr> <tr> <td>Anxiety</td> <td>~3.0</td> <td>~6.0</td> <td>$P < 0.04$</td> </tr> <tr> <td>Obsessive compulsive</td> <td>~3.5</td> <td>~6.5</td> <td>$P < 0.01$</td> </tr> </tbody> </table> <p>Control Abdominal pain</p> <p>Campo JV et al. Pediatrics 2001; 108:E1</p> <p>P72</p>	Category	Control (Blue)	Abdominal pain (Yellow)	P-value	Somatization	~3.5	~5.5	$P < 0.06$	Global severity	~1.0	~1.5	$P < 0.006$	Phobic activity	~1.0	~2.0	$P < 0.001$	Anxiety	~3.0	~6.0	$P < 0.04$	Obsessive compulsive	~3.5	~6.5	$P < 0.01$
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<p>P73</p>	<p>Prognostic Indicators in Children with Severe Functional Abdominal Pain (FAP)</p>	<p>Pediatrics Prognostic Indicators in Children with Severe Functional Abdominal Pain (FAP)</p> <p>Poor outcome (continued pain and failure to return to normal functioning 12 months after onset) was associated with:</p> <p>Lack of insight into psychosocial influences on symptoms RR 7.49</p> <p>Refusal to engage with psychological services RR 4.55</p> <p>Involvement of > 3 consultants RR 7.00</p> <p>Lodging of a manipulative complaint RR 3.25</p>  <p>R Lindley KJ et al. Arch Dis Child 2005; 90:335</p> <p>P73</p>
<p>P74</p>	<p>Hypnotherapy in Children with FAP-Slide 1 of 2</p>	<p>Pediatrics Hypnotherapy in Children with FAP</p>  <p>Mean pain-intensity score</p> <p>$P < 0.002$</p> <p>Standard medical therapy</p> <p>Hypnotherapy</p> <p>Treatment period</p> <p>start wk 1 wk 4 wk 8 wk 12 6 mo f/u 12 mo f/u</p> <p>R Villegier A et al. Gastroenterology 2007; 133:1430</p> <p>P74</p>
<p>P75</p>	<p>Hypnotherapy in Children with FAP-Improvement After Therapy-Slide 1 of 2</p>	<p>Pediatrics Improvement After Therapy for FAP or IBS</p> <p>SMT = Standard Medical Therapy HT = Hypnotherapy</p>  <p>%</p> <p>No effect Improved Asymptomatic</p> <p>*$P < 0.001$</p> <p>SMT HT</p> <p>After therapy (3 months) 1 year follow-up</p> <p>R Villegier A, et al. Gastroenterology 2007</p> <p>P75</p>

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<p>P76</p>	<p><i>Lactobacillus GG</i> for Abdominal Pain in Children</p>	<p>Pediatrics</p> <p><i>Lactobacillus GG</i> for Abdominal Pain</p> <table border="1"> <caption>Approximate data for <i>Lactobacillus GG</i> for Abdominal Pain</caption> <thead> <tr> <th>Group</th> <th>Treatment</th> <th>No effect (%)</th> <th>Improved (%)</th> <th>Asymptomatic (%)</th> </tr> </thead> <tbody> <tr> <td rowspan="2">FAP (n = 47)</td> <td>Placebo</td> <td>~30</td> <td>~55</td> <td>~15</td> </tr> <tr> <td>LGG (3x10⁹ bid)</td> <td>~25</td> <td>~40</td> <td>~35</td> </tr> <tr> <td rowspan="2">IBS (n = 37)</td> <td>Placebo</td> <td>~60</td> <td>~25</td> <td>~15</td> </tr> <tr> <td>LGG (3x10⁹ bid)</td> <td>~10</td> <td>~50</td> <td>~40</td> </tr> </tbody> </table> <p>Gawrońska AM et al. <i>Aliment Pharmacol Ther</i> 2007; 25:177</p> <p>P76</p>	Group	Treatment	No effect (%)	Improved (%)	Asymptomatic (%)	FAP (n = 47)	Placebo	~30	~55	~15	LGG (3x10 ⁹ bid)	~25	~40	~35	IBS (n = 37)	Placebo	~60	~25	~15	LGG (3x10 ⁹ bid)	~10	~50	~40
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<p>P77</p>	<p>Peppermint Oil in IBS in Children</p>	<p>Pediatrics</p> <p>Peppermint Oil in Pediatric IBS</p> <p>Menthol: Ca⁺⁺ channel-blocking activity</p> <table border="1"> <caption>Approximate data for Peppermint Oil in Pediatric IBS</caption> <thead> <tr> <th>Group</th> <th>Improvement (%)</th> </tr> </thead> <tbody> <tr> <td>Peppermint</td> <td>~75</td> </tr> <tr> <td>Placebo</td> <td>~40</td> </tr> </tbody> </table> <p>Kilinc RB et al. <i>J Pediatr</i> 2001; 138:125</p> <p>P77</p>	Group	Improvement (%)	Peppermint	~75	Placebo	~40																	
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<p>P78</p>	<p>Pain-Associated Disability Syndrome (PADS)</p>	<p>Pediatrics</p> <p>Pain-Associated Disability Syndrome (PADS)</p> <ul style="list-style-type: none"> • Factors associated with PADS included: <ul style="list-style-type: none"> • Disordered sleep • Learning disabilities • Unrealistic goals in a perfectionist, high-achieving child • Early pain experiences • Passive or dependent coping style • Family problems in the home • Chronic illness in a parent • Invasive procedures and surgery reinforce the cycle of arousal and pain <p>Hyman PE et al. <i>J Pediatr Gastroenterol Nutr</i> 2002; 35:663</p> <p>P78</p>																							

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<p>P79</p>	<p>Pediatric Functional Dyspepsia: Diagnostic Criteria</p>	<p>Pediatrics</p> <p>Functional Dyspepsia Diagnostic criteria* Must include all of the following:</p> <ul style="list-style-type: none"> • Persistent or recurrent pain or discomfort centered in the upper abdomen (above the umbilicus) • Not relieved by defecation or associated with the onset of a change in stool frequency or stool form (i.e. not IBS) • No evidence of an inflammatory, anatomic, metabolic or neoplastic process that explains the subject's symptoms <p>* Criteria fulfilled at least once per week for at least 2 months prior to diagnosis</p> <p>R P79</p>												
<p>P80</p>	<p>Accommodation is Abnormal in 53% of Dyspeptic Children</p>	<p>Pediatrics</p> <p>Accommodation is Abnormal in 53% of Dyspeptic Children</p> <table border="1"> <thead> <tr> <th>SPECT</th> <th>Fasting</th> <th>Postprandial</th> <th>Postprandial fasting ratio</th> </tr> </thead> <tbody> <tr> <td>Health</td> <td></td> <td></td> <td>3.90</td> </tr> <tr> <td>Functional dyspepsia</td> <td></td> <td></td> <td>1.72</td> </tr> </tbody> </table> <p>$P < 0.005$</p> <p>R Chilkara DK et al. J Pediatr 2005; 146:500 P80</p>	SPECT	Fasting	Postprandial	Postprandial fasting ratio	Health			3.90	Functional dyspepsia			1.72
SPECT	Fasting	Postprandial	Postprandial fasting ratio											
Health			3.90											
Functional dyspepsia			1.72											
<p>P81</p>	<p>Pediatric Functional Constipation: Diagnostic Criteria</p>	<p>Pediatrics</p> <p>Functional Constipation Diagnostic criteria*</p> <p>At least a 2 month history of at least two of the following 6 criteria:</p> <ol style="list-style-type: none"> 1) Two or fewer defecations in the toilet per week 2) At least one episode of fecal incontinence per week 3) History of retentive posturing or excessive volitional stool retention 4) History of painful or hard bowel movements 5) Presence of a large fecal mass in the rectum 6) History of large diameter stools that may obstruct the toilet <p>*Criteria fulfilled at least once per week for at least 2 months prior to diagnosis</p> <p>R P81</p>												


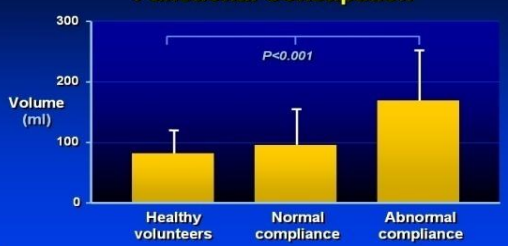
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<p>P82</p>	<p>Role of Genetics in Constipated Children</p>	<p>Pediatrics</p> <p>Role of Genetics in Constipated Children</p> <table border="1"> <caption>Role of Genetics in Constipated Children</caption> <thead> <tr> <th>Genetic Factor</th> <th>Percentage (%)</th> </tr> </thead> <tbody> <tr> <td>Dizygotic Twins</td> <td>~18</td> </tr> <tr> <td>Monozygotic Twins</td> <td>~70</td> </tr> <tr> <td>No parent constipated</td> <td>~5</td> </tr> <tr> <td>One parent constipated</td> <td>~12</td> </tr> <tr> <td>Both parents constipated</td> <td>~48</td> </tr> </tbody> </table> <p>Bakwin H et al. Am J Dis Child 1971; 121:179</p> <p>P82</p>	Genetic Factor	Percentage (%)	Dizygotic Twins	~18	Monozygotic Twins	~70	No parent constipated	~5	One parent constipated	~12	Both parents constipated	~48																																																																																										
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<p>P83</p>	<p>Age of Onset for Constipation</p>	<p>Pediatrics</p> <p>Age of Onset for Constipation</p> <p>When most vulnerable:</p> <ul style="list-style-type: none"> • Change in diet (weaning, introduction of solid foods) • Toilet training • School (Children too involved in their play, no bathroom breaks, lack of privacy or cleanliness of the bathroom) <p>P83</p>																																																																																																						
<p>P84</p>	<p>Population-Based Age Distribution of the Prevalence of Childhood Constipation</p>	<p>Pediatrics</p> <p>Population-Based Age Distribution of the Prevalence of Childhood Constipation</p> <table border="1"> <caption>Population-Based Age Distribution of the Prevalence of Childhood Constipation</caption> <thead> <tr> <th>Age (years)</th> <th>Loening-Baucke (%)</th> <th>Uguralp, et al. (%)</th> <th>Kajiwara, et al. (%)</th> <th>Yong and Beattie, et al. (%)</th> <th>Roma - Giannikou, et al. (%)</th> </tr> </thead> <tbody> <tr><td>0.2</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr> <tr><td>0.5</td><td>10</td><td>0</td><td>0</td><td>0</td><td>0</td></tr> <tr><td>1</td><td>15</td><td>0</td><td>0</td><td>0</td><td>0</td></tr> <tr><td>2</td><td>12</td><td>5</td><td>0</td><td>0</td><td>0</td></tr> <tr><td>3</td><td>15</td><td>10</td><td>0</td><td>0</td><td>0</td></tr> <tr><td>4</td><td>25</td><td>10</td><td>0</td><td>0</td><td>0</td></tr> <tr><td>5</td><td>28</td><td>10</td><td>0</td><td>0</td><td>0</td></tr> <tr><td>6</td><td>15</td><td>10</td><td>0</td><td>0</td><td>0</td></tr> <tr><td>7</td><td>12</td><td>10</td><td>0</td><td>0</td><td>0</td></tr> <tr><td>8</td><td>10</td><td>10</td><td>20</td><td>0</td><td>0</td></tr> <tr><td>9</td><td>10</td><td>10</td><td>18</td><td>0</td><td>0</td></tr> <tr><td>10</td><td>10</td><td>10</td><td>15</td><td>0</td><td>0</td></tr> <tr><td>11</td><td>10</td><td>10</td><td>15</td><td>0</td><td>0</td></tr> <tr><td>12</td><td>10</td><td>10</td><td>15</td><td>0</td><td>0</td></tr> <tr><td>13</td><td>10</td><td>10</td><td>15</td><td>0</td><td>0</td></tr> <tr><td>14</td><td>10</td><td>10</td><td>15</td><td>0</td><td>0</td></tr> </tbody> </table> <p>van den Berg MM et al. Am J Gastroenterol 2006; 101:2401</p> <p>P84</p>	Age (years)	Loening-Baucke (%)	Uguralp, et al. (%)	Kajiwara, et al. (%)	Yong and Beattie, et al. (%)	Roma - Giannikou, et al. (%)	0.2	0	0	0	0	0	0.5	10	0	0	0	0	1	15	0	0	0	0	2	12	5	0	0	0	3	15	10	0	0	0	4	25	10	0	0	0	5	28	10	0	0	0	6	15	10	0	0	0	7	12	10	0	0	0	8	10	10	20	0	0	9	10	10	18	0	0	10	10	10	15	0	0	11	10	10	15	0	0	12	10	10	15	0	0	13	10	10	15	0	0	14	10	10	15	0	0
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P85	Cow Milk Intolerance and Chronic Constipation in Children	<p>Pediatrics</p> <h3>Cow Milk Intolerance and Chronic Constipation in Children</h3> <p>Crossover</p> <table border="1"><thead><tr><th>Group</th><th>Cow's milk</th><th>Soy milk</th></tr></thead><tbody><tr><td>No response</td><td>33</td><td>10</td></tr><tr><td>Response (≥ 8 BMs/2weeks)</td><td>20</td><td>22</td></tr></tbody></table> <p>Legend: No response (green), Response (≥ 8 BMs/2weeks) (yellow)</p> <p>lacono G et al. <i>N Engl J Med</i> 1998; 339:1100</p> <p>P85</p>	Group	Cow's milk	Soy milk	No response	33	10	Response (≥ 8 BMs/2weeks)	20	22	
Group	Cow's milk	Soy milk										
No response	33	10										
Response (≥ 8 BMs/2weeks)	20	22										
P86	Pediatric Functional Constipation: Parents' Reported Quality of Life	<p>Pediatrics</p> <h3>Functional Constipation Parents' Reported Quality of Life</h3> <table border="1"><thead><tr><th>Group</th><th>Pediatric QOL score (0-100)</th></tr></thead><tbody><tr><td>HC</td><td>88</td></tr><tr><td>IBD</td><td>75</td></tr><tr><td>GERD</td><td>77</td></tr><tr><td>CONS</td><td>62</td></tr></tbody></table> <p>Legend: HC (blue), IBD (orange), GERD (green), CONS (red)</p> <p>Youssef NN et al. <i>J Pediatr Gastroenterol Nutr</i> 2005; 41:56</p> <p>P86</p>	Group	Pediatric QOL score (0-100)	HC	88	IBD	75	GERD	77	CONS	62
Group	Pediatric QOL score (0-100)											
HC	88											
IBD	75											
GERD	77											
CONS	62											
P87	Retentive Posturing	<p>P87</p>										

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<p>P88</p>	<p>Symptoms of Pediatric Functional Constipation</p>	<p>Pediatrics</p> <p>Symptoms of Functional Constipation</p> <p>(%)</p> <table border="1"> <tr> <td>Fecal incontinence</td> <td>75 - 90</td> </tr> <tr> <td>Defecation frequency < 3/wk</td> <td>75</td> </tr> <tr> <td>Large fecal mass</td> <td>75</td> </tr> <tr> <td>Straining during defecation</td> <td>35</td> </tr> <tr> <td>Pain during defecation</td> <td>50 - 80</td> </tr> <tr> <td>Withholding posture</td> <td>35 - 45</td> </tr> <tr> <td>Abdominal pain</td> <td>10 - 70</td> </tr> </table> <p>R Van der Plas RN et al. Lancet 1996; 348:776</p> <p>P88</p>	Fecal incontinence	75 - 90	Defecation frequency < 3/wk	75	Large fecal mass	75	Straining during defecation	35	Pain during defecation	50 - 80	Withholding posture	35 - 45	Abdominal pain	10 - 70
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Abdominal pain	10 - 70															
<p>P89</p>	<p>Long-Term Pediatric Functional Constipation</p>	<p>Pediatrics</p> <p>Long-Term Functional Constipation</p>  <p>Fecal impaction</p> <p>Increased rectal compliance and decreased motor function</p> <p>R Voskuil WP, et al. J Pediatr 2006; 148:62</p> <p>P89</p>														
<p>P90</p>	<p>Volume at Urge to Defecate in Children with Functional Constipation</p>	<p>Pediatrics</p> <p>Volume at Urge to Defecate in Children with Functional Constipation</p>  <p>Volume (ml)</p> <p>Healthy volunteers Normal compliance Abnormal compliance</p> <p>$P < 0.001$</p> <p>R Voskuil WP et al. J Pediatr 2006; 148:62</p> <p>P90</p>														

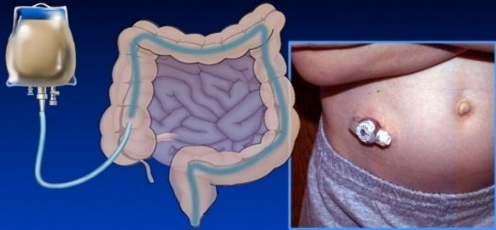
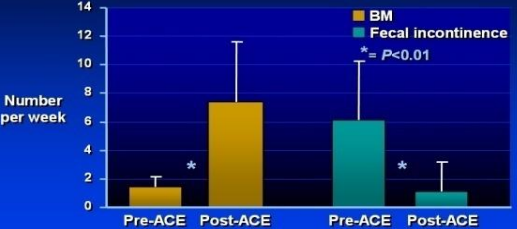
Computer-Based Learning Program
Pediatric

<p>P91</p>	<p>Disimpaction: Dose Response to PEG 3350-Pediatric</p>	<p>Pediatrics</p> <p>Disimpaction: Dose Response to PEG 3350</p> <table border="1"> <caption>Disimpaction: Dose Response to PEG 3350</caption> <thead> <tr> <th>Dose (grams/kg/day x 3 days)</th> <th>% Patients disimpacted</th> </tr> </thead> <tbody> <tr> <td>0.25</td> <td>~60</td> </tr> <tr> <td>0.5</td> <td>~40</td> </tr> <tr> <td>1.0</td> <td>~90*</td> </tr> <tr> <td>1.5</td> <td>~100*</td> </tr> </tbody> </table> <p><small>Youssef NN et al. J Pediatr 2002; 141:410</small></p> <p><small>P91</small></p>	Dose (grams/kg/day x 3 days)	% Patients disimpacted	0.25	~60	0.5	~40	1.0	~90*	1.5	~100*					
Dose (grams/kg/day x 3 days)	% Patients disimpacted																
0.25	~60																
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1.0	~90*																
1.5	~100*																
<p>P92</p>	<p>Effect of PEG 3350 With Electrolytes vs Lactulose-Pediatric</p>	<p>Pediatrics</p> <p>Effect of PEG 3350 With Electrolytes vs Lactulose</p> <table border="1"> <caption>Effect of PEG 3350 With Electrolytes vs Lactulose</caption> <thead> <tr> <th>Category</th> <th>Baseline</th> <th>8 weeks later</th> </tr> </thead> <tbody> <tr> <td>Defecation PEG 3350</td> <td>~3</td> <td>~6*</td> </tr> <tr> <td>Defecation Lactulose</td> <td>~3</td> <td>~6*</td> </tr> <tr> <td>Fecal incontinence PEG 3350</td> <td>~10</td> <td>~3*</td> </tr> <tr> <td>Fecal incontinence Lactulose</td> <td>~8</td> <td>~3*</td> </tr> </tbody> </table> <p><small>Voskuyl WP et al. Gut 2004; 53:1590</small></p> <p><small>P92</small></p>	Category	Baseline	8 weeks later	Defecation PEG 3350	~3	~6*	Defecation Lactulose	~3	~6*	Fecal incontinence PEG 3350	~10	~3*	Fecal incontinence Lactulose	~8	~3*
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<p>P93</p>	<p>Effect of PEG 3350 vs Milk of Magnesia-Pediatric</p>	<p>Pediatrics</p> <p>Effect of PEG 3350 vs Milk of Magnesia</p> <table border="1"> <caption>Effect of PEG 3350 vs Milk of Magnesia</caption> <thead> <tr> <th>Follow-up</th> <th>PEG (Recovered + Improved)</th> <th>MOM (Recovered + Improved)</th> </tr> </thead> <tbody> <tr> <td>1 month</td> <td>~48%</td> <td>~55%</td> </tr> <tr> <td>3 month</td> <td>~48%</td> <td>~50%</td> </tr> <tr> <td>6 month</td> <td>~45%</td> <td>~45%</td> </tr> <tr> <td>12 month</td> <td>~42%</td> <td>~42%</td> </tr> </tbody> </table> <p><small>Loening-Baucke V et al. Pediatrics 2006; 118:528</small></p> <p><small>P93</small></p>	Follow-up	PEG (Recovered + Improved)	MOM (Recovered + Improved)	1 month	~48%	~55%	3 month	~48%	~50%	6 month	~45%	~45%	12 month	~42%	~42%
Follow-up	PEG (Recovered + Improved)	MOM (Recovered + Improved)															
1 month	~48%	~55%															
3 month	~48%	~50%															
6 month	~45%	~45%															
12 month	~42%	~42%															

Computer-Based Learning Program
Pediatric

<p>P94</p>	<p>Biofeedback Training: Defecation Disorders-Pediatric-Part 1</p>	<p>Pediatrics Biofeedback Training: Defecation Disorders Abnormal Rectal pressure Anal canal pressure Increase P94</p>															
<p>P95</p>	<p>Biofeedback Training: Defecation Disorders-Pediatric-Part 2</p>	<p>Pediatrics Biofeedback Training: Defecation Disorders Normal Rectal pressure Anal canal pressure Decrease P95</p>															
<p>P96</p>	<p>Anorectal Biofeedback in Childhood Constipation</p>	<p>Pediatrics Anorectal Biofeedback in Childhood Constipation</p> <table border="1"> <thead> <tr> <th>Time Point</th> <th>Conventional therapy (CT) (n = 94) (%)</th> <th>Conventional therapy + Biofeedback (n = 98) (%)</th> </tr> </thead> <tbody> <tr> <td>6 weeks</td> <td>~30</td> <td>~30</td> </tr> <tr> <td>6 months</td> <td>~50</td> <td>~45</td> </tr> <tr> <td>1 year</td> <td>~55</td> <td>~48</td> </tr> <tr> <td>1.5 years</td> <td>~55</td> <td>~42</td> </tr> </tbody> </table> <p>NS Van der Plas RN et al. Lancet 1996; 348:776 P96</p>	Time Point	Conventional therapy (CT) (n = 94) (%)	Conventional therapy + Biofeedback (n = 98) (%)	6 weeks	~30	~30	6 months	~50	~45	1 year	~55	~48	1.5 years	~55	~42
Time Point	Conventional therapy (CT) (n = 94) (%)	Conventional therapy + Biofeedback (n = 98) (%)															
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Computer-Based Learning Program
Pediatric

<p>P97</p>	<p>Treating Childhood Constipation</p>	<p>Pediatrics</p> <p>Treating Childhood Constipation</p> <ul style="list-style-type: none"> • Fear of painful defecation must be eliminated by softening stools to assure painless defecation • Rectum must be emptied of impacted stool until fear is gone and reliable bowel habit is established. This may take a long time! • Incontinence is associated with fecal impaction • Prolonged maintenance treatment and successful toilet training are essential before drugs are discontinued <p>R</p> <p>P97</p>									
<p>P98</p>	<p>Cecostomy</p>	<p>Pediatrics</p> <p>Cecostomy</p>  <p>R</p> <p>P98</p>									
<p>P99</p>	<p>Effect of Antegrade Colonic Enemas (ACE) in Children with Constipation</p>	<p>Pediatrics</p> <p>Effect of Antegrade Colonic Enemas (ACE) in Children with Constipation</p>  <table border="1"> <caption>Effect of Antegrade Colonic Enemas (ACE) in Children with Constipation</caption> <thead> <tr> <th>Parameter</th> <th>Pre-ACE</th> <th>Post-ACE</th> </tr> </thead> <tbody> <tr> <td>BM (Number per week)</td> <td>~1.5</td> <td>~7.5</td> </tr> <tr> <td>Fecal incontinence (Number per week)</td> <td>~6</td> <td>~1</td> </tr> </tbody> </table> <p>R</p> <p>Youssef NN et al. J Pediatr Gastroenterol Nutr 2002; 34:402</p> <p>P99</p>	Parameter	Pre-ACE	Post-ACE	BM (Number per week)	~1.5	~7.5	Fecal incontinence (Number per week)	~6	~1
Parameter	Pre-ACE	Post-ACE									
BM (Number per week)	~1.5	~7.5									
Fecal incontinence (Number per week)	~6	~1									

Computer-Based Learning Program
Pediatric

<p>P100</p>	<p>Outcome of Child Constipation-Part 1</p>	<p>Pediatrics</p> <p>Outcome of Childhood Constipation</p> <p>van Ginkel R et al. Gastroenterology 2003; 125:357</p> <p>P100</p>
<p>P101</p>	<p>Outcome of Child Constipation-Part 2</p>	<p>Pediatrics</p> <p>Outcome of Childhood Constipation</p> <p>van Ginkel R et al. Gastroenterology 2003; 125:357</p> <p>P101</p>
<p>P102</p>	<p>Nonretentive Fecal Incontinence: Diagnostic Criteria</p>	<p>Pediatrics</p> <p>Nonretentive Fecal Incontinence</p> <p>Diagnostic criteria: Must include all of the following in a child with a developmental age of at least 4 years:</p> <ul style="list-style-type: none"> • Defecation into places inappropriate to the social context at least once per month • No evidence of an inflammatory, anatomic, metabolic or neoplastic process that explains the subject's symptoms • No evidence of fecal retention <p>*Criteria fulfilled for at least two months prior to diagnosis</p> <p>P102</p>

Computer-Based Learning Program
Pediatric

<p>P103</p>	<p>Achievement of Bowel Control in Children</p>	<p>Pediatrics</p> <p>Achievement of Bowel Control</p> <p>n = 349 healthy term infants</p> <table border="1"> <thead> <tr> <th>Months</th> <th>Start of toilet training (%)</th> <th>Toilet trained for feces (%)</th> </tr> </thead> <tbody> <tr> <td>12</td> <td>20</td> <td>5</td> </tr> <tr> <td>24</td> <td>60</td> <td>10</td> </tr> <tr> <td>36</td> <td>90</td> <td>60</td> </tr> <tr> <td>48</td> <td>95</td> <td>90</td> </tr> </tbody> </table> <p>Largo RH et al. Eur J Pediatr 1999; 158:115</p> <p>P103</p>	Months	Start of toilet training (%)	Toilet trained for feces (%)	12	20	5	24	60	10	36	90	60	48	95	90												
Months	Start of toilet training (%)	Toilet trained for feces (%)																											
12	20	5																											
24	60	10																											
36	90	60																											
48	95	90																											
<p>P104</p>	<p>Prevalence of Fecal Incontinence in Children</p>	<p>Pediatrics</p> <p>Prevalence of Fecal Incontinence</p> <ul style="list-style-type: none"> • School children <ul style="list-style-type: none"> • 7 years old 1-2% • 10-12 years old 1.3% • Male predominance 6:1 <p>Bellman M. Acta Pediatr Scand 1966; 170:1</p> <p>Children Taken to a Doctor for Evaluation</p> <ul style="list-style-type: none"> • 5-6 years old 38% • 11-12 years old 27% <p>Van der Wal MF et al. J Pediatr Gastroenterol Nutr 2005; 40:345</p> <p>P104</p>																											
<p>P105</p>	<p>Features of Nonretentive Fecal Incontinence (NRFI)</p>	<p>Pediatrics</p> <p>Features of Nonretentive Fecal Incontinence vs Functional Constipation</p> <table border="1"> <thead> <tr> <th>Feature</th> <th>NRFI (%)</th> <th>FC (%)</th> </tr> </thead> <tbody> <tr> <td>Boys</td> <td>90</td> <td>90</td> </tr> <tr> <td>Large stool</td> <td>10</td> <td>60</td> </tr> <tr> <td>Night-time fecal incontinence</td> <td>10</td> <td>35</td> </tr> <tr> <td>Pain during defecation</td> <td>20</td> <td>50</td> </tr> <tr> <td>Abdominal pain</td> <td>20</td> <td>40</td> </tr> <tr> <td>Urinary incontinence</td> <td>40</td> <td>20</td> </tr> <tr> <td>Palpable abdominal mass</td> <td>30</td> <td>35</td> </tr> <tr> <td>Palpable rectal mass</td> <td>30</td> <td>35</td> </tr> </tbody> </table> <p>Bennings MA et al. Arch Dis Child 1994; 71:186</p> <p>P105</p>	Feature	NRFI (%)	FC (%)	Boys	90	90	Large stool	10	60	Night-time fecal incontinence	10	35	Pain during defecation	20	50	Abdominal pain	20	40	Urinary incontinence	40	20	Palpable abdominal mass	30	35	Palpable rectal mass	30	35
Feature	NRFI (%)	FC (%)																											
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Urinary incontinence	40	20																											
Palpable abdominal mass	30	35																											
Palpable rectal mass	30	35																											

Computer-Based Learning Program
Pediatric

<p>P106</p>	<p>Symptoms in Nonretentive Fecal Incontinence (NRFI)</p>	<p>Pediatrics</p> <p>Symptoms in Nonretentive Fecal Incontinence (NRFI)</p> <table border="1"> <thead> <tr> <th></th> <th>C n = 129 %</th> <th>NRFI n = 54 %</th> </tr> </thead> <tbody> <tr> <td>Normal transit time</td> <td>52</td> <td>91</td> </tr> <tr> <td>Hindgut dysfunction</td> <td>6</td> <td>0</td> </tr> <tr> <td>Outlet obstruction</td> <td>32</td> <td>9</td> </tr> <tr> <td>Slow transit constipation</td> <td>10</td> <td>0</td> </tr> </tbody> </table> <p>R Benninga MA et al. Eur J Pediatr 1995; 154:277</p> <p>P 106</p>		C n = 129 %	NRFI n = 54 %	Normal transit time	52	91	Hindgut dysfunction	6	0	Outlet obstruction	32	9	Slow transit constipation	10	0
	C n = 129 %	NRFI n = 54 %															
Normal transit time	52	91															
Hindgut dysfunction	6	0															
Outlet obstruction	32	9															
Slow transit constipation	10	0															
<p>P107</p>	<p>Functional Nonretentive Fecal Incontinence: Treatment Options</p>	<p>Pediatrics</p> <p>Treatment Options</p> <p>R Bongers ME et al. J Pediatr Gastroenterol Nutr 2007; 44:5</p> <p>P 107</p>															
<p>P108</p>	<p>Outcome of Nonretentive Fecal Incontinence (NRFI) After Behavioral Therapy</p>	<p>Pediatrics</p> <p>Outcome of Nonretentive Fecal Incontinence (NRFI) After Behavioral Therapy</p> <p>R Voskuilij WP et al. Clin Gastroenterol Hepatol 2006; 4:67</p> <p>P 108</p>															

Computer-Based Learning Program
Pediatric

P109	Outcome of Childhood NRFI	<p>Pediatrics</p> <h3>Outcome of Childhood NRFI</h3> <table border="1"><thead><tr><th>Age (years)</th><th>% success</th></tr></thead><tbody><tr><td>6</td><td>20</td></tr><tr><td>7</td><td>15</td></tr><tr><td>8</td><td>20</td></tr><tr><td>9</td><td>25</td></tr><tr><td>10</td><td>35</td></tr><tr><td>11</td><td>38</td></tr><tr><td>12</td><td>50</td></tr><tr><td>13</td><td>58</td></tr><tr><td>14</td><td>62</td></tr><tr><td>15</td><td>65</td></tr><tr><td>16</td><td>72</td></tr><tr><td>17</td><td>85</td></tr><tr><td>18</td><td>82</td></tr></tbody></table> <p>Voskuilj WP et al. Clin Gastroenterol Hepatol 2006; 4:67</p> <p>P109</p>	Age (years)	% success	6	20	7	15	8	20	9	25	10	35	11	38	12	50	13	58	14	62	15	65	16	72	17	85	18	82
Age (years)	% success																													
6	20																													
7	15																													
8	20																													
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10	35																													
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13	58																													
14	62																													
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16	72																													
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18	82																													
P110	Nonretentive Fecal Incontinence	<p>Pediatrics</p> <h3>Nonretentive Fecal Incontinence</h3> <ul style="list-style-type: none">• After 2 years of intensive behavioral and medical therapy, <30% are successfully treated• Cumulative success reaches 80% after 12 years of follow-up• At 18 years, 15% still have fecal incontinence• Relapse occurs frequently and most likely in the first 2 years after successful treatment• Intensive monitoring and follow-up are necessary <p>P110</p>																												

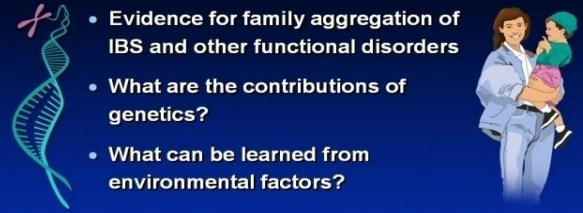
Computer-Based Learning Program
Psychosocial

Slide Number	Slide Title
Ps1	Nature and Nurture
Ps2	Evidence for Influence of Social Learning Over Genetics in Twin Study
Ps3	Children of IBS Patients Make More Health Care Visits for GI Symptoms

Childhood and Genetic Factors - FGIDs


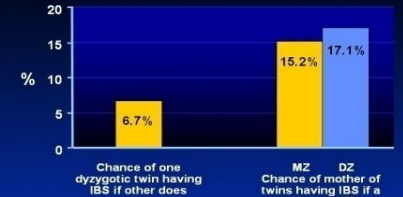
Nature and Nurture

- Evidence for family aggregation of IBS and other functional disorders
- What are the contributions of genetics?
- What can be learned from environmental factors?



Ps1

Evidence for Influence of Social Learning over Genetics in Twin Study





Category	Value (%)
Chance of one dizygotic twin having IBS if other does	6.7%
MZ (Chance of mother of twins having IBS if a twin has IBS)	15.2%
DZ (Chance of mother of twins having IBS if a twin has IBS)	17.1%

Levy RL et al. Gastroenterology, 2001; 121:799

Ps2

Children of IBS Patients Make More Healthcare Visits for GI Symptoms



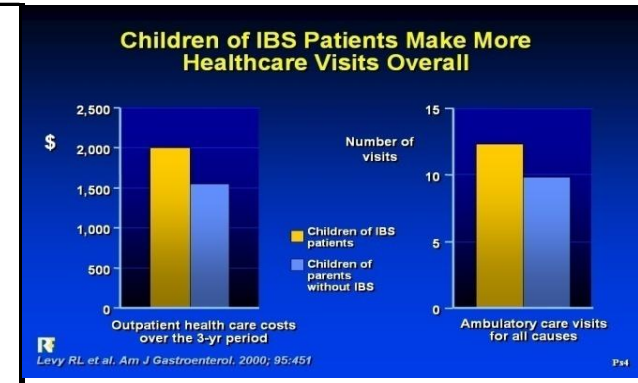
GI Symptom	Children of IBS patients (%)	Children of parents without IBS (%)
Diarrhea	~9%	~3%
Abdominal Pain	~12%	~6%
Any GI Visits	~21%	~10%

Levy RL et al. Am J Gastroenterol, 2000; 95:451

Ps3

Computer-Based Learning Program
Psychosocial

Ps4 Children of IBS Patients Make More Health Care Visits Overall



Ps5 Effect of Family Life Events and Mothers' Somatic Symptoms on Children's FGID Symptom Outcomes-Slide 1 of 4

Effect of Family Life Events and Mothers' Somatic Symptoms on Children's FGID Symptom Outcomes

Predictive variables	β	T	R ² change
Step 1: Control variables			
Age			.12***
Socioeconomic status	0.07	1.0	
Time I CSI (child symptoms)	0.09	1.34	
Diagnostic group	.27	3.87**	
Organic pain	-.08	-1.09	
Specific pain syndrome	.04	.22	
			P<.01 *P<.001

Walker LS et al. J Consult Clin Psych. 1994; 62:1213

Ps6 Effect of Family Life Events and Mothers' Somatic Symptoms on Children's FGID Symptom Outcomes-Slide 2 of 4

Effect of Family Life Events and Mothers' Somatic Symptoms on Children's FGID Symptom Outcomes

Predictive variables	β	T	R ² change
Step 1: Control variables			
			.12***
Step 2: Predictor variables			
Family life events	.09	2.77**	.03***
Mother's somatic symptoms	.16	2.29	
Sex	.02	.29	
			P<.01 *P<.001

Walker LS et al. J Consult Clin Psych. 1994; 62:1213

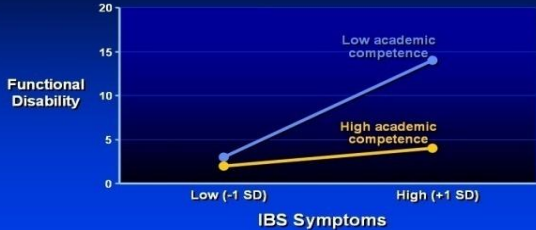
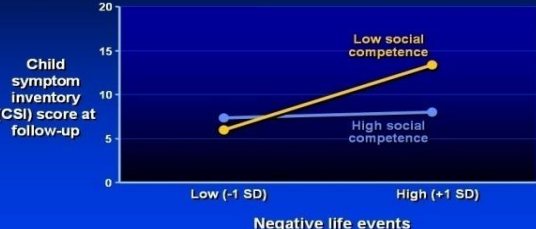
Computer-Based Learning Program
Psychosocial

<p>Ps7</p>	<p>Effect of Family Life Events and Mothers' Somatic Symptoms on Children's FGID Symptom Outcomes-Slide 3 of 4</p>	<p>Effect of Family Life Events and Mothers' Somatic Symptoms on Children's FGID Symptom Outcomes</p> <table border="1"> <thead> <tr> <th>Predictive variables</th> <th>β</th> <th>T</th> <th>R² change</th> </tr> </thead> <tbody> <tr> <td>Step 1: Control variables</td> <td></td> <td></td> <td>.12***</td> </tr> <tr> <td>Step 2: Predictor variables</td> <td></td> <td></td> <td>.07***</td> </tr> <tr> <td>Step 3: 2-way interactions</td> <td></td> <td></td> <td>.03</td> </tr> <tr> <td>Life events X Mother's somatic symptoms</td> <td>.11</td> <td>.66</td> <td></td> </tr> <tr> <td>Life events X Sex</td> <td>-.31</td> <td>-2.57***</td> <td></td> </tr> <tr> <td>Sex X Mother's somatic symptoms</td> <td>-.06</td> <td>-.54</td> <td></td> </tr> </tbody> </table> <p>***p<.001</p> <p>R Walker LS et al. <i>J Consult Clin Psych</i>. 1994; 62:1213 P17</p>	Predictive variables	β	T	R ² change	Step 1: Control variables			.12***	Step 2: Predictor variables			.07***	Step 3: 2-way interactions			.03	Life events X Mother's somatic symptoms	.11	.66		Life events X Sex	-.31	-2.57***		Sex X Mother's somatic symptoms	-.06	-.54	
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<p>Ps8</p>	<p>Effect of Family Life Events and Mothers' Somatic Symptoms on Children's FGID Symptom Outcomes-Slide 4 of 4</p>	<p>Effect of Family Life Events and Mothers' Somatic Symptoms on Children's FGID Symptom Outcomes</p> <table border="1"> <thead> <tr> <th>Predictive variables</th> <th>β</th> <th>T</th> <th>R² change</th> </tr> </thead> <tbody> <tr> <td>Step 1: Control variables</td> <td></td> <td></td> <td>.12***</td> </tr> <tr> <td>Step 2: Predictor variables</td> <td></td> <td></td> <td>.07***</td> </tr> <tr> <td>Step 3: 2-way interactions</td> <td></td> <td></td> <td>.03</td> </tr> <tr> <td>Step 4: 3-way interactions</td> <td></td> <td></td> <td>.04***</td> </tr> <tr> <td>Sex X Life events X Mother's somatic symptoms</td> <td>-.79</td> <td>-3.32***</td> <td></td> </tr> </tbody> </table> <p>***p<.001</p> <p>R Walker LS et al. <i>J Consult Clin Psych</i>. 1994; 62:1213 P18</p>	Predictive variables	β	T	R ² change	Step 1: Control variables			.12***	Step 2: Predictor variables			.07***	Step 3: 2-way interactions			.03	Step 4: 3-way interactions			.04***	Sex X Life events X Mother's somatic symptoms	-.79	-3.32***					
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Step 4: 3-way interactions			.04***																											
Sex X Life events X Mother's somatic symptoms	-.79	-3.32***																												
<p>Ps9</p>	<p>Associations Between Maternal Reinforcement and Seriousness of Stomach Ache-Slide 1 of 2</p>	<p>Associations Between Maternal Reinforcement and Seriousness of Stomach Ache</p> <table border="1"> <thead> <tr> <th>Level of maternal reinforcement</th> <th>Seriousness of stomach ache (approx.)</th> </tr> </thead> <tbody> <tr> <td>Low</td> <td>3.2</td> </tr> <tr> <td>Middle</td> <td>3.8</td> </tr> <tr> <td>High</td> <td>4.1</td> </tr> </tbody> </table> <p>R Levy RL et al. <i>Am J Gastroenterol</i> 2004; 99:2442 P19</p>	Level of maternal reinforcement	Seriousness of stomach ache (approx.)	Low	3.2	Middle	3.8	High	4.1																				
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<p>Ps10</p>	<p>Associations Between Maternal Reinforcement and Parental IBS, and Illness Behavior-Slide 2 of 2</p>	<p>Associations Between Maternal Reinforcement and Parental IBS, and Illness Behavior</p> <p> $p < 0.001$ for parent status $p < 0.05$ for illness reinforcement </p> <p>School absences for GI 3 months</p> <p>Low Middle High Parents without IBS Low Middle High Parents with IBS</p> <p><small>Levy RL et al. Am J Gastroenterol, 2004; 99:2442</small></p> <p><small>Ps10</small></p>
<p>Ps11</p>	<p>Associations Between Distraction and Amount of Symptom Talk in Laboratory Setting</p>	<p>Associations Between Distraction and Amount of Symptom Talk in Laboratory Setting</p> <p> ■ Pain patients ■ Well children </p> <p>Child Symptom Talk</p> <p>Distraction No Instruction Attention</p> <p><small>Walker LS et al. Pain 2006; 122:43</small> <small>Walker LS et al. J Pediatr Psychol, 2006; 31:703</small></p> <p><small>Ps11</small></p>
<p>Ps12</p>	<p>Parents Can Help Maximize Wellness Behaviors in Their Children</p>	<p>Parents Can Help Maximize Wellness Behaviors in Their Children</p> <ul style="list-style-type: none"> • Model appropriate responses to physical symptoms • Reward healthy adaptive behaviors • Avoid providing children with rewards for inappropriate symptom complaints • Use distraction, avoid negativity <p><small>Ps12</small></p>

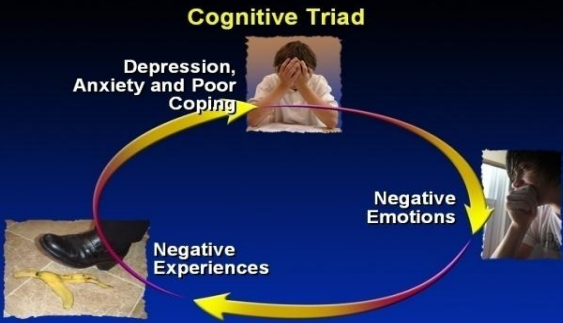
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<p>Ps13</p>	<p>Associations Between Outcomes in FGIDs and Psychological Background in Adolescents</p>	<p>Associations Between Outcomes in FGIDs and Psychological Background in Adolescents</p> <ul style="list-style-type: none"> • Risk factors for poor outcomes <ul style="list-style-type: none"> • Child and family stressors • Child anxiety/depression • Pain threat cognitions • Passive coping with pain • Protective factors <ul style="list-style-type: none"> • Child social competence • Child self-esteem <p><small>Ps13</small></p>									
<p>Ps14</p>	<p>Academic Success Protects from More Severe Symptoms</p>	<p>Academic Success Protects from More Severe Symptoms</p>  <p>The graph plots Functional Disability (y-axis, 0-20) against IBS Symptoms (x-axis, Low (-1 SD) to High (+1 SD)). Two lines represent different levels of academic competence. The 'Low academic competence' line (blue) shows a steep increase in disability as symptoms increase. The 'High academic competence' line (yellow) shows a much flatter, lower increase in disability for the same symptom increase.</p> <table border="1"> <caption>Approximate data for Ps14 graph</caption> <thead> <tr> <th>IBS Symptoms</th> <th>Low academic competence (Functional Disability)</th> <th>High academic competence (Functional Disability)</th> </tr> </thead> <tbody> <tr> <td>Low (-1 SD)</td> <td>~3</td> <td>~2</td> </tr> <tr> <td>High (+1 SD)</td> <td>~14</td> <td>~4</td> </tr> </tbody> </table> <p><small>Ps14</small></p>	IBS Symptoms	Low academic competence (Functional Disability)	High academic competence (Functional Disability)	Low (-1 SD)	~3	~2	High (+1 SD)	~14	~4
IBS Symptoms	Low academic competence (Functional Disability)	High academic competence (Functional Disability)									
Low (-1 SD)	~3	~2									
High (+1 SD)	~14	~4									
<p>Ps15</p>	<p>Social Competence Moderates Effect of Stress on IBS Symptoms</p>	<p>Social Competence Moderates Effect of Stress on IBS Symptoms</p>  <p>The graph plots Child symptom inventory (CSI) score at follow-up (y-axis, 0-20) against Negative life events (x-axis, Low (-1 SD) to High (+1 SD)). Two lines represent different levels of social competence. The 'Low social competence' line (yellow) shows a steep increase in CSI score as negative life events increase. The 'High social competence' line (blue) shows a much flatter, lower increase in CSI score for the same event increase.</p> <table border="1"> <caption>Approximate data for Ps15 graph</caption> <thead> <tr> <th>Negative life events</th> <th>Low social competence (CSI score)</th> <th>High social competence (CSI score)</th> </tr> </thead> <tbody> <tr> <td>Low (-1 SD)</td> <td>~6</td> <td>~7</td> </tr> <tr> <td>High (+1 SD)</td> <td>~14</td> <td>~8</td> </tr> </tbody> </table> <p><small>Ps15</small></p>	Negative life events	Low social competence (CSI score)	High social competence (CSI score)	Low (-1 SD)	~6	~7	High (+1 SD)	~14	~8
Negative life events	Low social competence (CSI score)	High social competence (CSI score)									
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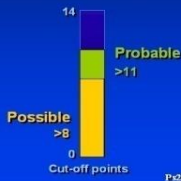
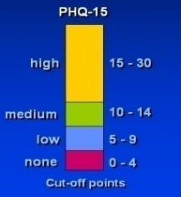
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<p>Ps16</p>	<p>Relationships Among Risk Factors and Outcomes in Children with FAP</p>	<p>Relationships Among Risk Factors and Outcomes in Children with FAP</p> <pre> graph TD subgraph Clinic PC[Passive Coping with Pain] PTC[Pain Threat Cognitions] PC <--> r = .43** PTC end subgraph 3_months [3 months (Phone)] S[Symptoms r = .43***] D[Disability r = .46**] Dep[Depression r = .50**] end PC --> S PC --> D PC --> Dep PTC --> S PTC --> D PTC --> Dep </pre> <p>Walker LS et al. <i>Health Psychology</i>, 2005 24(4):364</p> <p>Ps16</p>
<p>Ps17</p>	<p>Sexual and Physical Abuse</p>	<p>Sexual and Physical Abuse</p> <ul style="list-style-type: none"> • High frequency rates of abuse reported in the U.S. and Europe • High frequencies of childhood abuse • Patients with abuse histories report: <ul style="list-style-type: none"> • More severe pain • Greater psychological distress • Greater functional impairment • More frequent visits to the doctor <p>Drossman DA et al. <i>Gastroenterology</i> 1996; 110:999</p> <p>Ps17</p>
<p>Ps18</p>	<p>Stressful Events Predict: Onset of FGIDs, Symptom exacerbation & health seeking, & IBS symptom intensity</p>	<p>Stressful Events Predict</p> <ul style="list-style-type: none"> • Onset of FGIDs • Symptom exacerbation and health seeking • IBS symptom intensity <p>Bennett EJ et al. <i>Gut</i> 1998; 43:256 Creed FH et al. <i>Gut</i> 1988; 29:235</p> <p>Ps18</p>




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Ps19	Cognitive Triad	 <p>Cognitive Triad</p> <p>Depression, Anxiety and Poor Coping</p> <p>Negative Experiences</p> <p>Negative Emotions</p> <p>Ps19</p>
Ps20	Health Beliefs & Coping-FGIDs-Cognitions	<p>Health Beliefs and Coping - FGIDs</p> <p>Cognitions</p> <ul style="list-style-type: none">• Catastrophizing The tendency to exaggerate the threat of certain symptoms• GI-specific anxiety Heightened sensitivity to, and fear of, anxiety-related GI sensations• Health anxiety Worry about bodily symptoms• Selective attention to thoughts and perceptions that confirm patients' understandings and concerns about GI symptoms <p>Ps20</p>
Ps21	Psychosocial Assessment Toolkit-Slide 1 of 2	<p>Psychosocial Assessment - FGIDs</p> <p>Psychosocial Assessment Toolkit</p> <ul style="list-style-type: none">• Hospital Anxiety and Depression Scale Mood (anxiety and depression) screening• Patient Health Questionnaire-15 Reporting of multiple bodily symptoms• Coping Strategies Questionnaire, Catastrophizing Scale Inability to cope with or disengage from symptoms <p>Ps21</p>





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<p>Ps22</p>	<p>Psychosocial Assessment Toolkit-Slide 2 of 2</p>	<p>Psychosocial Assessment Toolkit</p> <ul style="list-style-type: none"> • Visceral Sensitivity Index GI specific anxiety • IBS-Quality Of Life IBS specific quality of life – IBS-QOL • Structured Clinical Interview for DSM IV Diagnostic interview – primarily for research <p>Mini-International Neuropsychiatric Interview Brief diagnostic interview – primarily for research</p> <p><small>Pr22</small></p>
<p>Ps23</p>	<p>Depression and Anxiety Screening: Hospital Anxiety and Depression Scale (HADS)</p>	<p>Depression and Anxiety Screening Hospital Anxiety and Depression Scale (HADS)</p> <ul style="list-style-type: none"> • Used in FGID studies and other medical populations • Probably most widely used and well-validated tool • 14 items <ul style="list-style-type: none"> • 7-anxiety • 7-depression • Good for screening, not diagnosis • Sensitive to treatment  <p><small>Pr23</small></p>
<p>Ps24</p>	<p>Multiple Symptom Screening: Patient Health Questionnaire-15 (PHQ-15)</p>	<p>Multiple Symptom Screening Patient Health Questionnaire-15 (PHQ-15)</p> <ul style="list-style-type: none"> • 15 items scored on a 3 point scale of bothersomeness (total possible=30) • Scores are correlated with ratings of functional disability and number of physician visits • Scores are associated with diagnosis of somatization disorder • Should be used as measure of breadth and severity of physical symptoms, not somatization <i>per se</i>  <p><small>Pr24</small></p>

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Ps25	Catastrophizing Screening: Coping Strategies Questionnaire-Catastrophizing Scale (CSQ-C)	<p>Catastrophizing Screening: Coping Strategies Questionnaire Catastrophizing Scale (CSQ-C)</p> <ul style="list-style-type: none">• 6 subscales with 53 items on coping with painful conditions• Catastrophizing subscale is a 6 item scale covering illness fear, worry and pessimism• Catastrophizing correlates best with the negative sequelae of chronic pain• Perceived Control and Ability to Decrease Pain are single item scales used as predictors of adverse health outcomes <p> Keefe FJ et al. Pain;1989; 37:51 Ps25</p>
Ps26	Symptom-Specific Anxiety: Visceral Sensitivity Index (VSI)	<p>Symptom-Specific Anxiety Visceral Sensitivity Index (VSI)</p> <ul style="list-style-type: none">• 15 items• GI Symptom anxiety includes:<ul style="list-style-type: none">• Worry, fear, vigilance, sensitivity, and avoidance behavior related to visceral sensations and their context• VSI more uniquely related to IBS symptoms than general anxiety measures• May be useful as both an assessment and outcome measure in IBS <p> Labus JS et al. Aliment Pharmacol Ther. 2004; 20:89 Ps26</p>
Ps27	Screening for IBS-Specific Quality of Life: IBS QOL	<p>Screening for IBS-Specific Quality of Life: IBS QOL</p> <ul style="list-style-type: none">• 34 item self-report questionnaire• 8 subscales:<ul style="list-style-type: none">• Dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, sexual relationship• Good psychometric validation and most widely used IBS QOL-specific measure <p> Patrick DL et al. Dig Dis Sci. 1998; 43:400 Ps27</p>

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Ps28	Structured Clinical Interview for DSM (SCID)	<p>Structured Clinical Interview for DSM (SCID)</p> <ul style="list-style-type: none">• Most widely used and validated tool for all Axis I and II diagnoses• From 45 min to >2 hrs to complete depending on number of positive findings and number of diagnostic modules used• Specific training is required to use properly• Good correlation between diagnoses made by SCID interview and by experienced clinicians <p> Spitzer RL et al. Structured Clinical Interview for DSM-III-R. Am Psychiatr Assoc Press, 1990 Ps28</p>
Ps29	Mini-International Neuropsychiatric Interview (MINI)	<p>Mini-International Neuropsychiatric Interview (MINI)</p> <ul style="list-style-type: none">• Brief structured interview for the major Axis I psychiatric disorders in DSM-IV and ICD-10• High reliability and validity compared to SCID and requires less time• Brevity, clarity, ease of administration, high sensitivity, and high specificity• Requires little training• Available in long forms (MINI+) or brief screening format <p> Sheehan DV et al. J Clin Psychiatry 1998; 59 Suppl 20:22 Ps29</p>
Ps30	IBS - Patient's Agenda	<p>IBS - Patient's Agenda</p>  <p>The illustration shows a woman in a purple top and dark skirt standing next to a brown door. She has several thought bubbles above her head, each containing a question or concern: "Do I have cancer?", "My symptoms are worse", "They think it's all in my head", "I'm under more stress", "Why am I not getting better?", "Will you believe me?", and "Am I crazy?".</p> <p> Ps30</p>


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<p>Ps31</p>	<p>IBS - Doctor's Agenda</p>	<p>IBS - Doctor's Agenda</p>
<p>Ps32</p>	<p>A Typical Scenario: Physician Reaction</p>	<p>A Typical Scenario → Physician Reaction</p> <ul style="list-style-type: none"> • Bizarre complaint • Vague pain complaint • Nothing works Allergic! <ul style="list-style-type: none"> • "This person is nuts" • Despair / anger • Diagnosis/treatment paralysis <p>Solution: Biopsychosocial Approach</p>
<p>Ps33</p>	<p>Psychological Comorbidity: Let's Get Focused</p>	<p>Doctor-Patient Relationship - FGIDs</p> <p>Psychological Comorbidity Let's Get Focused</p> <p>Nuts (crazy)</p> <ul style="list-style-type: none"> • Is not a medical term • Reinforces physician powerlessness • Cannot treat what you cannot describe

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Ps34	Psychological Comorbidity: Approach	<p>Doctor-Patient Relationship - FGIDs</p> <p>Psychological Comorbidity: Approach</p> <ol style="list-style-type: none">1. Acknowledge burden of illness2. Screen for psychiatric comorbidity<ul style="list-style-type: none">• Use rating scales – easy, objective3. Quantify psychiatric patterns <p>Ps34</p>
Ps35	What the Doctor Says - What the Patient Hears	<p>Doctor-Patient Relationship - FGIDs</p> <p>What the Doctor Says: What the Patient Hears:</p>  <p>Just to be sure . . .</p> <p>You may have IBS . . .</p> <p>Nothing to worry about . . .</p> <p>Cancer?</p> <p>Cancer?</p> <p>Cancer?</p> <p>Cancer?</p> <p>Ps35</p>
Ps36	Common Psychiatric Diagnoses in FGIDs	<p>Common Psychiatric Diagnoses in FGIDs</p> <ul style="list-style-type: none">• Mood (depressive) disorders• Anxiety disorders• Somatoform disorders <p>Ps36</p>


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<p>Ps37</p>	<p>Anxiety Disorders</p>	<p style="text-align: center;">Anxiety Disorders</p> <ul style="list-style-type: none"> • Panic disorder • Generalized anxiety disorder • Post traumatic stress disorder  <p style="text-align: right;">Ps37</p>																														
<p>Ps38</p>	<p>A Treatment Algorithm for Patients with FGIDs</p>	<p style="text-align: center;">Severity → Symptom severity Psych distress Disability Previous therapy</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 33%;">Mild (common)</th> <th style="width: 33%;">Moderate</th> <th style="width: 33%;">Severe (uncommon)</th> </tr> </thead> <tbody> <tr> <td>Positive physician/patient interaction Education: understanding of illness</td> <td></td> <td></td> </tr> <tr> <td>Symptomatic medical treatment</td> <td colspan="2">Cognitive behavioral treatment, interpersonal therapy stress management /relaxation, hypnosis exercise, relaxation</td> </tr> <tr> <td>Psychopharmacology</td> <td></td> <td></td> </tr> <tr> <td>Low-dose or TCA</td> <td></td> <td></td> </tr> <tr> <td>SSRI / SNRI</td> <td></td> <td></td> </tr> <tr> <td>4-6 weeks Monitor side effects</td> <td></td> <td></td> </tr> <tr> <td></td> <td>Adjust dosage</td> <td>Psychiatric Consultation</td> </tr> <tr> <td></td> <td>4-6 weeks Monitor side effects</td> <td>Combination behavior and psychopharmacology</td> </tr> <tr> <td></td> <td></td> <td>Switch or Add 2nd drug</td> </tr> </tbody> </table> <p style="text-align: right;">Ps38</p>	Mild (common)	Moderate	Severe (uncommon)	Positive physician/patient interaction Education: understanding of illness			Symptomatic medical treatment	Cognitive behavioral treatment, interpersonal therapy stress management /relaxation, hypnosis exercise, relaxation		Psychopharmacology			Low-dose or TCA			SSRI / SNRI			4-6 weeks Monitor side effects				Adjust dosage	Psychiatric Consultation		4-6 weeks Monitor side effects	Combination behavior and psychopharmacology			Switch or Add 2 nd drug
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<p>Ps39</p>	<p>Red Flags – Mental Health Consultation</p>	<p style="text-align: center;">Severity → Symptom severity Psych distress Disability Previous therapy</p> <p>Red Flags Mental Health Consultation</p> <ul style="list-style-type: none"> • Severe depression / suicidal • Chronic refractory pain • Severe disability • Maladaptive illness behavior • Difficulties in physician – patient interaction • Idiosyncratic health beliefs • Other identifiable psychological difficulties (somatization disorder, PTSD, severe anxiety, abuse) <p style="text-align: right;">Ps39</p>																														


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Ps40	Targets for Psychological Treatment of FGIDs	<p>Targets for Psychological Treatment of FGIDs</p> <ul style="list-style-type: none">Maladaptive Disease Model<ul style="list-style-type: none">• Maladaptive beliefsOveractive Stress Response<ul style="list-style-type: none">• Response to general stress• Response to FGID symptomsMaladaptive Psychological Adjustment<ul style="list-style-type: none">• Catastrophizing• Symptom specific anxiety• Sick-role• Shame/guiltMaladaptive Behaviors<ul style="list-style-type: none">• Avoidance• Safety seeking <p>Ⓡ Ps40</p>
Ps41	Psychological Treatment Components	<p>Psychological Treatment Components</p> <ul style="list-style-type: none">• Education• Relaxation• Cognitive change• General stress coping• Behavioral change <p>Ⓡ Ps41</p>
Ps42	Barriers to Psychotherapy	<p>Barriers to Psychotherapy</p> <ul style="list-style-type: none">• Provider Training• Availability Care• Costs of Care<ul style="list-style-type: none">• Duration of Treatment• Financial <p>Ⓡ Ps42</p>

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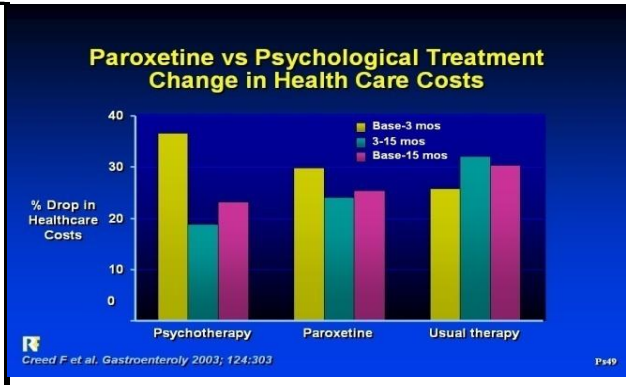
<p>Ps43</p>	<p>Cognitive Behavioral Therapy</p>	<p>Psychological Treatments - FGIDs</p> <ul style="list-style-type: none">• Addresses thoughts, behaviors, and responses that result from patients' experiences <p>Cognitive Behavioral Therapy</p> <ul style="list-style-type: none">• Relaxation/stress management• Helps patients to recognize relationship between beliefs and symptoms <p>Ps43</p>
<p>Ps44</p>	<p>Hypnotherapy</p>	<p>Hypnotherapy</p>  <p>Image: A calm river</p> <p>Refocus: No pain</p> <p>Heightened suggestibility</p> <p>Rough water: Severe pain</p> <p>Heavy focus on pain</p> <p>Can't cope</p> <p>Ps44</p>
<p>Ps45</p>	<p>Psychodynamic Interpersonal Therapy</p>	<p>Psychological Treatments - FGIDs</p> <ul style="list-style-type: none">• The relationship between the patient and the therapist is used as the primary vehicle for change <p>Psychodynamic Interpersonal Therapy</p> <ul style="list-style-type: none">• Focuses on factors within relationships that contribute to the persistence of pain and the chronicity of symptoms <p>Ps45</p>

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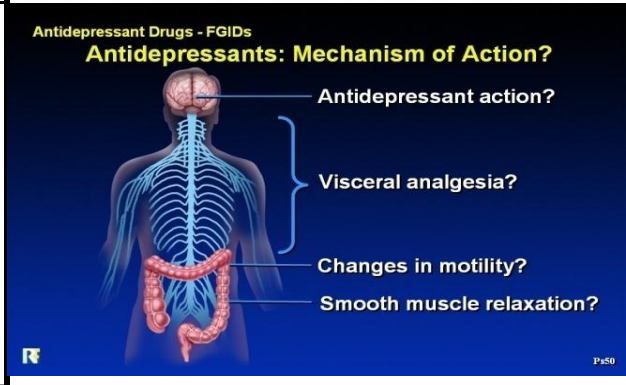
Ps46	Response to Psychological Treatment: Women versus Men	<p>Psychological Treatments - FGIDs</p> <p>Response to Psychological Treatment: Women versus Men</p> <ul style="list-style-type: none">• Most psychological treatment trials in FGID have not been powered to examine different response patterns• Most studies have recruited more females than males (average ratio 3:1) <p>Ⓡ Ps46</p>												
Ps47	Future Research Directions	<p>Psychological Treatments - FGIDs</p> <p>Future Research Directions</p> <ul style="list-style-type: none">• Effectiveness studies of psychological treatment<ul style="list-style-type: none">• Combined psychological and pharmacological treatment• Application in primary care• Minimal contact strategies• Subgroup responses to treatment<ul style="list-style-type: none">• Sex• Culture• Extent of co-morbidity• Mechanistic studies linking psychosocial factors to symptom expression and outcomes <p>Ⓡ Ps47</p>												
Ps48	Paroxetine vs Psychological Treatment-Slide 1 of 2	<p>Paroxetine vs Psychological Treatment</p>  <table border="1"><thead><tr><th>Outcome</th><th>Psychotherapy</th><th>Paroxetine</th><th>Usual therapy</th></tr></thead><tbody><tr><td>Pain</td><td>~52</td><td>~50</td><td>~50</td></tr><tr><td>HRQOL</td><td>~44</td><td>~42</td><td>~38</td></tr></tbody></table> <p>Ⓡ Creed F et al. Gastroenterology 2003; 124:303 Ps48</p>	Outcome	Psychotherapy	Paroxetine	Usual therapy	Pain	~52	~50	~50	HRQOL	~44	~42	~38
Outcome	Psychotherapy	Paroxetine	Usual therapy											
Pain	~52	~50	~50											
HRQOL	~44	~42	~38											

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Ps49 Paroxetine vs Psychological Treatment Change in Health Care Costs-Slide 2 of 2



Ps50 Antidepressants: Mechanism of Action?



Ps51 TCA Receptor Activity

Antidepressant Drugs - FGIDs
TCA Receptor Activity




TCA	NE	5-HT	H ₁	Ach
Amitriptyline	++	++	++++	++++
Imipramine	++	++	++++	++
Desipramine	++++	++	+	+
Nortriptyline	+++	++	++	++

Ps51









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Ps52	SSRI Antidepressant Receptor Activity	<p>Antidepressant Drugs - FGIDs</p> <h3>SSRI Antidepressant Receptor Activity</h3> <p>SSRI's</p> <ul style="list-style-type: none">• All have 5-HT effect only• Except paroxetine which has mild Ach effect <p>℞</p> <p>Ps52</p>												
Ps53	SNRI Antidepressant Receptor Activity	<p>Antidepressant Drugs - FGIDs</p> <h3>SNRI Antidepressant Receptor Activity</h3> <table border="1"><thead><tr><th>SNRIs</th><th>NE</th><th>5-HT</th><th>Ach</th></tr></thead><tbody><tr><td>Venlafaxine</td><td>++</td><td>+++</td><td>0</td></tr><tr><td>Duloxetine</td><td>++++</td><td>++++</td><td>0</td></tr></tbody></table> <p>℞</p> <p>Ps53</p>	SNRIs	NE	5-HT	Ach	Venlafaxine	++	+++	0	Duloxetine	++++	++++	0
SNRIs	NE	5-HT	Ach											
Venlafaxine	++	+++	0											
Duloxetine	++++	++++	0											
Ps54	Tricyclic Antidepressant (TCA) Dosing	<p>Antidepressant Drugs - FGIDs</p> <h3>Tricyclic Antidepressant (TCA) Dosing</h3> <ul style="list-style-type: none">• All TCAs have similar doses• Usual dose is 10-150 mg q.h.s• Dose should be titrated by side effect <p>℞</p> <p>Ps54</p>												

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<p>Ps55</p>	<p>SSRI: Dosing Guidelines</p>	<p>Antidepressant Drugs - FGIDs</p> <p>SSRI: Dosing Guidelines</p> <table border="1"> <thead> <tr> <th>Antidepressant</th> <th>GI Dosage (mg)</th> <th>Range (mg/d)</th> </tr> </thead> <tbody> <tr> <td>Fluoxetine (<i>Prozac</i>)</td> <td>10-20</td> <td>20-80</td> </tr> <tr> <td>Fluvoxamine (<i>Luvox</i>)</td> <td>25-50</td> <td>50-300</td> </tr> <tr> <td>Paroxetine (<i>Paxil</i>)</td> <td>10-20</td> <td>20-50</td> </tr> <tr> <td>Sertraline (<i>Zoloft</i>)</td> <td>25-50</td> <td>50-200</td> </tr> <tr> <td>Venlafaxine (<i>Effexor</i>)</td> <td>10-20</td> <td>75-375</td> </tr> </tbody> </table> <p> Ps55</p>	Antidepressant	GI Dosage (mg)	Range (mg/d)	Fluoxetine (<i>Prozac</i>)	10-20	20-80	Fluvoxamine (<i>Luvox</i>)	25-50	50-300	Paroxetine (<i>Paxil</i>)	10-20	20-50	Sertraline (<i>Zoloft</i>)	25-50	50-200	Venlafaxine (<i>Effexor</i>)	10-20	75-375
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Venlafaxine (<i>Effexor</i>)	10-20	75-375																		
<p>Ps56</p>	<p>Anti-anxiety or Antidepressants for Functional Dyspepsia: A Systematic Review</p>	<p>Antidepressant Drugs - FGIDs</p> <p>Anti-Anxiety or Anti-Depressants for Functional Dyspepsia: A Systematic Review</p> <ul style="list-style-type: none"> • 13 RCTs (1717 patients) • 11/13 trials showed benefit • 4 trials included in a formal statistical analysis <table border="1"> <thead> <tr> <th></th> <th>Anti-depressants (3) or Anxiolytics (1)</th> <th>Anti-depressants (3)</th> </tr> </thead> <tbody> <tr> <td>Relative risk (95% CI)</td> <td>0.55 (0.36-0.85)</td> <td>0.42 (0.29-0.61)</td> </tr> </tbody> </table> <p> <i>Hojo et al. J Gastroenterology 2005; 40:1036</i> Ps56</p>		Anti-depressants (3) or Anxiolytics (1)	Anti-depressants (3)	Relative risk (95% CI)	0.55 (0.36-0.85)	0.42 (0.29-0.61)												
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<p>Ps57</p>	<p>Psychotropic Drug Treatment: Females vs Males in FGIDs</p>	<p>Antidepressant Drugs - FGIDs</p> <p>Psychotropic Drug Treatment: Females vs Males in FGID</p> <ul style="list-style-type: none"> • No systematic review or meta-analysis of psychotropic drug treatment in FGIDs has included a gender analysis • Pharmacological studies of psychotropic drugs in FGIDs <ul style="list-style-type: none"> • Are small • Most participants are female • No data on gender differences in response to psychotropic agents in FGID <p> Ps57</p>																		

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<p>Ps58</p>	<p>Sex, Gender, and Gender Role</p>	<p>Sex, Gender, and Gender Role</p> <p>Sex  Biological femaleness or maleness</p> <p>Gender  Nonbiological aspects of being male or female; social expectations associated with femininity or masculinity</p> <p>Gender Role  Characteristics and behaviour that are based on sex stereotypes</p> <p> Ps58</p>																												
<p>Ps59</p>	<p>Key Characteristics of Sex Stereotypes in Western Culture</p>	<p>Key Characteristics of Sex Stereotypes in Western Culture</p> <p>Femininity </p> <p>Expressive, relationship-oriented, dependent, submissive, emotional, nurturing, intuitive</p> <p>Masculinity </p> <p>Competency-oriented, independent, rational, competitive, providing, objective</p> <p> Ps59</p>																												
<p>Ps60</p>	<p>Gender Differences in Psychological Distress in FGIDs</p>	<p>Gender Differences in Psychological Distress in FGID</p> <table border="1"> <thead> <tr> <th>Study</th> <th>No.</th> <th>Setting and recruitment</th> <th>Findings</th> </tr> </thead> <tbody> <tr> <td>Corney and Stanton, 1990</td> <td>42</td> <td>Outpatients</td> <td>Females > males for psychological distress</td> </tr> <tr> <td>Blewett, 1996</td> <td>76</td> <td>Outpatients</td> <td>Females = males</td> </tr> <tr> <td>Simren, 2001</td> <td>343</td> <td>Outpatients and primary care patients</td> <td>Females > males for fatigue, depression and anxiety</td> </tr> <tr> <td>Lee, 2001</td> <td>714</td> <td>Outpatients</td> <td>Females = males</td> </tr> <tr> <td>Blanchard, 2001</td> <td>341</td> <td>IBS patients who sought non-drug tx</td> <td>Females > males for depression Females = males for anxiety</td> </tr> <tr> <td>Westbrook, 2002</td> <td>748</td> <td>Population based</td> <td>Females > males re poorer mental well-being</td> </tr> </tbody> </table> <p> Ps60</p>	Study	No.	Setting and recruitment	Findings	Corney and Stanton, 1990	42	Outpatients	Females > males for psychological distress	Blewett, 1996	76	Outpatients	Females = males	Simren, 2001	343	Outpatients and primary care patients	Females > males for fatigue, depression and anxiety	Lee, 2001	714	Outpatients	Females = males	Blanchard, 2001	341	IBS patients who sought non-drug tx	Females > males for depression Females = males for anxiety	Westbrook, 2002	748	Population based	Females > males re poorer mental well-being
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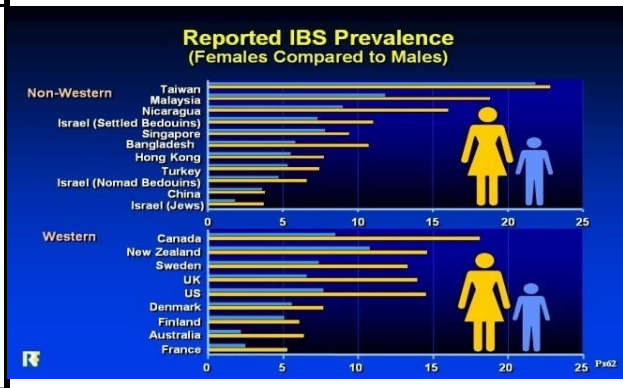
Ps61
Gender & Psychosocial Factors - Summary

Gender & Psychosocial Factors - Summary

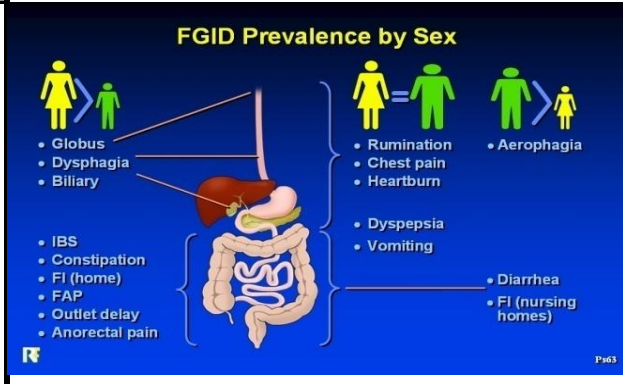
- Few studies examined these factors
- No major differences between males and females with FGIDs in terms of psychological profile
- Few studies have included sufficient males to be able to make valid comparison between the genders

Ps61

Ps62
Reported IBS Prevalence: Females Compared to Males

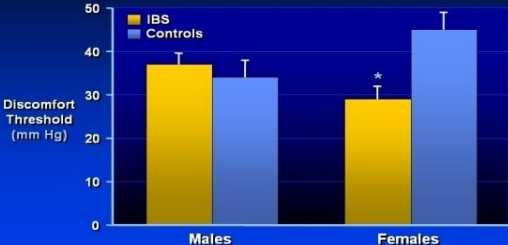
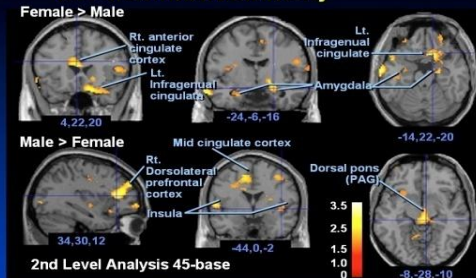


Ps63
FGID Prevalence by Sex

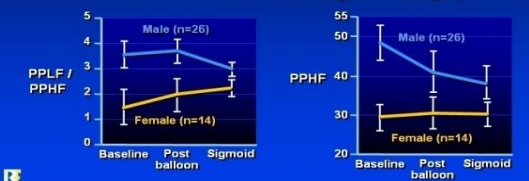
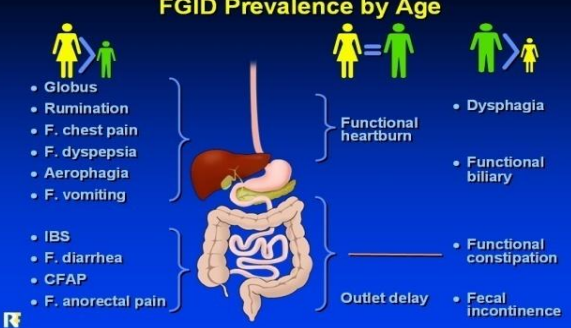


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<p>Ps64</p>	<p>Sex Differences in Visceral Pain in Healthy Humans-Slide 1 of 2</p>	<p>Sex Differences in Visceral Pain in Healthy Humans</p> <ul style="list-style-type: none"> • No significant sex-related differences in pressure thresholds in the esophagus,¹⁻² and duodenum³ • Greater increase in perceptual ratings to gastric distension in women vs. men⁴ • No significant sex differences in rectal pressure thresholds⁵ or perceptual ratings⁶ <p>• Limitations</p> <ul style="list-style-type: none"> • No control for menstrual cycle • Small sample sizes • Different psychophysiological paradigms <p><small>¹ Nguyen NO et al. Am J Gastro 1995; 90:901 ⁴Mearadji B et al. Am J Gastro 2001; 96:2066 ² Rao SS et al. Am J Gastro 2003; 98:1688 ⁵Sloots CE et al. Neurogastro Mot 2000; 12:361 ³ Holtmann G et al. A J Gastro 1997; 92:954 ⁶Soffer EE et al. Dig Dis Sci 2000; 45:1281</small></p>																								
<p>Ps65</p>	<p>Sex Differences in Visceral Pain in Healthy Humans-Slide 2 of 2</p>	<p>Sex Differences in Visceral Pain in Healthy Humans</p> <table border="1"> <thead> <tr> <th>Area</th> <th>Parameter tested</th> <th>Differences</th> <th>Study</th> </tr> </thead> <tbody> <tr> <td>Esophagus</td> <td>Pressure threshold</td> <td>none</td> <td>1, 2</td> </tr> <tr> <td>Duodenum</td> <td>Pressure threshold</td> <td>none</td> <td>3</td> </tr> <tr> <td>Stomach</td> <td>Perceptual rating</td> <td>W>M</td> <td>4</td> </tr> <tr> <td>Rectum</td> <td>Pressure threshold</td> <td>none</td> <td>5</td> </tr> <tr> <td>Rectum</td> <td>Perceptual rating</td> <td>none</td> <td>6</td> </tr> </tbody> </table> <p><small>¹ Nguyen NO et al. Am J Gastro 1995; 90:901 ⁴ Mearadji B et al. Am J Gastro 2001; 96:2066 ² Rao SS et al. Am J Gastro 2003; 98:1688 ⁵ Sloots CE et al. Neurogastro Mot 2000; 12:361 ³ Holtmann G et al. Am J Gastro 1997; 92:954 ⁶ Soffer EE et al. Dig Dis Sci 2000; 45:1281</small></p>	Area	Parameter tested	Differences	Study	Esophagus	Pressure threshold	none	1, 2	Duodenum	Pressure threshold	none	3	Stomach	Perceptual rating	W>M	4	Rectum	Pressure threshold	none	5	Rectum	Perceptual rating	none	6
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<p>Ps66</p>	<p>Sex Differences in Rectal Perception in IBS</p>	<p>Sex Differences in Rectal Perception in IBS</p> <ul style="list-style-type: none"> • Rectal sensitivity was assessed in 13 men and 39 women with IBS before and after a meal • Women showed a significant decrease in post-prandial rectal pressure thresholds of maximal tolerated distension compared to men <p><small>Ragnarsson et al. Scand J Gastroenterol 1999; 34:250</small></p>																								

<p>Ps67</p>	<p>Sex Differences in Visceral Sensitivity</p>	<p>Sex Differences in Visceral Sensitivity</p>  <table border="1"> <caption>Sex Differences in Visceral Sensitivity Data</caption> <thead> <tr> <th>Sex</th> <th>IBS (mm Hg)</th> <th>Controls (mm Hg)</th> </tr> </thead> <tbody> <tr> <td>Males</td> <td>~37</td> <td>~34</td> </tr> <tr> <td>Females</td> <td>~29*</td> <td>~45</td> </tr> </tbody> </table> <p>Chang L et al. <i>Am J Physiol Regul Integr Comp Physiol.</i> 2006; 291:R277</p> <p>Ps67</p>	Sex	IBS (mm Hg)	Controls (mm Hg)	Males	~37	~34	Females	~29*	~45
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<p>Ps68</p>	<p>Central Processing of Visceral Stimuli</p>	<p>Gender and Biological Factors - FGIDs</p> <p>Central Processing of Visceral Stimuli</p> <ul style="list-style-type: none"> • Few studies have addressed gender differences • In one neuroimaging study of IBS patients: <ul style="list-style-type: none"> • Men had greater activation of endogenous pain inhibition areas • Women had greater activation of pain facilitation areas • Men and women may process aversive information from the pelvic viscera differently <p>Naliboff B et al. <i>Gastroenterology</i> 2003; 124:1738</p> <p>Ps68</p>									
<p>Ps69</p>	<p>Men and Women May Process Aversive Information from the Pelvic Viscera Differently</p>	<p>Gender and Biological Factors - FGIDs</p> <p>Men and Women May Process Aversive Information from the Pelvic Viscera Differently</p> <p>Women had greater activation of pain facilitation areas</p> <p>Male > Female</p>  <p>Male > Female</p> <p>Men had greater activation of cognitive and pain inhibition areas</p> <p>2nd Level Analysis 45-base</p> <p>Naliboff et al. <i>Gastroenterology</i> 2003; 124:1738</p> <p>Ps69</p>									



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<p>Ps70</p>	<p>Cardioautonomic Tone Differs Between Men and Women with IBS</p>	<p>Cardioautonomic Tone Differs Between Men and Women with IBS</p> <p>One study showed that in response to rectosigmoid distension</p> <ul style="list-style-type: none"> • Men have greater cardiosympathetic tone (left) • Men have lower cardiovagal tone (right)  <p><i>Tillisch K et al. Gut 2005; 54:1396</i></p> <p>Ps70</p>
<p>Ps71</p>	<p>Social Factors</p>	<p>Social Factors</p> <p>Social determinants of health need to be incorporated into clinical practice</p> <p>These include:</p> <ul style="list-style-type: none"> • Stress • Early life • Addiction • Food • Socio-economic status • Work • Unemployment • Transportation • Social exclusion • Social support <p><i>World Health Organization 1998</i></p> <p>Ps71</p>
<p>Ps72</p>	<p>FGID Prevalence by Age</p>	<p>FGID Prevalence by Age</p>  <ul style="list-style-type: none"> • Globus • Rumination • F. chest pain • F. dyspepsia • Aerophagia • F. vomiting • IBS • F. diarrhea • CFAP • F. anorectal pain • Functional heartburn • Dysphagia • Functional biliary • Functional constipation • Fecal incontinence <p>Outlet delay</p> <p>Ps72</p>

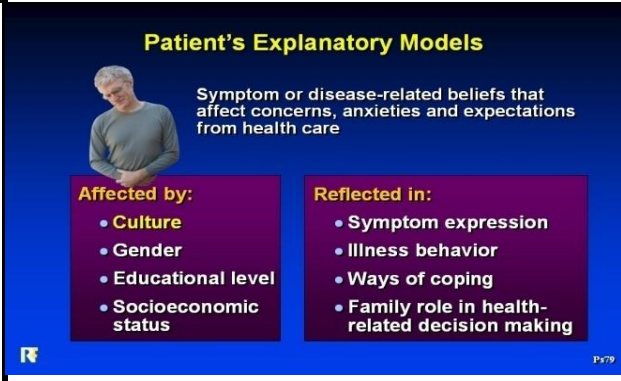
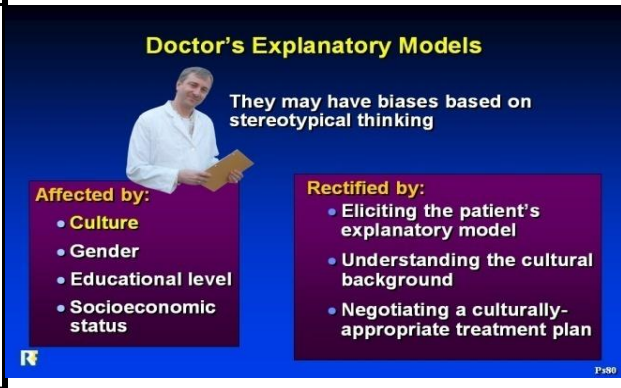
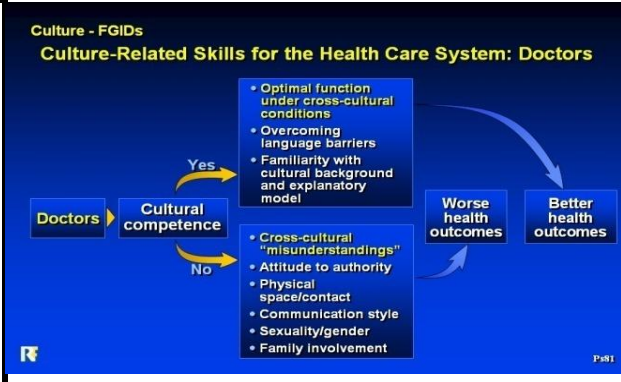
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Ps73	Living with Functional Gastrointestinal Disorders	<p>Living with Functional Gastrointestinal Disorders</p> <ul style="list-style-type: none">• Major interference with daily life• Social stigma and isolation• Intimate nature of symptoms• Perceived lack of validity• Inability to discuss with others• Long course with unpredictable symptom episodes   <p>R Ps73</p>
Ps74	Uncertainty of Living With FGIDs	<p>Uncertainty of Living With FGIDs</p> <ul style="list-style-type: none">• Absence of definitive biological marker• Lack of satisfactory treatment• Lack of certainty over symptom triggers, onset and severity• Inability to control symptoms<ul style="list-style-type: none">• Avoidance, withdrawal, vigilance, concealment <p>R Ps74</p>
Ps75	Patient-Physician Encounter	<p>Patient-Physician Encounter</p> <p>Patients may feel:</p> <ul style="list-style-type: none">• Lack of empathy• Explanation unhelpful• They are not partners in the treatment plan   <p>R Ps75</p>

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Ps76	Patient-Physician Partnership	<p>Patient-Physician Partnership</p> <p>Physicians need to provide clear explanations about:</p> <ul style="list-style-type: none">• The nature of the illness• Treatment goals and options  <p>Patients need to learn to:</p> <ul style="list-style-type: none">• Develop adaptive coping skills for chronic illness• Be less passive in their care <p><small>Ps76</small></p>
Ps77	Culture and Health Care	<p>Culture and Health Care</p> <ul style="list-style-type: none">• Culture is the shared values of a particular group that guide behavior• Ethnic disparities in death rates from all major diseases• Patients' race, ethnicity and sex influence physicians' recommendations concerning treatment <p><small>Dimsdale JE Psychosom Med. 2000; 62:161 Ng B et al. Pain 1996; 66:9</small></p> <p><small>Ps77</small></p>
Ps78	Lack of Awareness of Cultural Factors	 <pre>graph LR; A[Lack of awareness of cultural factors] --> Clinical practice B[Poor health outcomes]; A --> Research C[Methodological pitfalls];</pre> <p><small>Ps78</small></p>




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<p>Ps79</p>	<p>Patients' Explanatory Models</p>	 <p>Patient's Explanatory Models</p> <p>Symptom or disease-related beliefs that affect concerns, anxieties and expectations from health care</p> <p>Affected by:</p> <ul style="list-style-type: none"> • Culture • Gender • Educational level • Socioeconomic status <p>Reflected in:</p> <ul style="list-style-type: none"> • Symptom expression • Illness behavior • Ways of coping • Family role in health-related decision making <p>Ps79</p>
<p>Ps80</p>	<p>Doctors' Explanatory Models</p>	 <p>Doctor's Explanatory Models</p> <p>They may have biases based on stereotypical thinking</p> <p>Affected by:</p> <ul style="list-style-type: none"> • Culture • Gender • Educational level • Socioeconomic status <p>Rectified by:</p> <ul style="list-style-type: none"> • Eliciting the patient's explanatory model • Understanding the cultural background • Negotiating a culturally-appropriate treatment plan <p>Ps80</p>
<p>Ps81</p>	<p>Culture-Related Skills for the Health Care System: Doctors</p>	 <p>Culture - FGIDs</p> <p>Culture-Related Skills for the Health Care System: Doctors</p> <p>Doctors → Cultural competence</p> <p>Yes → Optimal function under cross-cultural conditions, Overcoming language barriers, Familiarity with cultural background and explanatory model</p> <p>No → Cross-cultural "misunderstandings", Attitude to authority, Physical space/contact, Communication style, Sexuality/gender, Family involvement</p> <p>Worse health outcomes → Better health outcomes</p> <p>Ps81</p>


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<p>Ps82</p>	<p>Culture-Related Skills for the Health Care System: Patients</p>	<p>Culture - FGIDs Culture-Related Skills for the Health Care System: Patients</p> <pre> graph LR Patients --> CC[Cultural competence] CC -- No --> Difficulties["• Difficulty in understanding • Diagnosis • Discharge instructions • Treatment • Leading to 'non-compliance' • Possible adverse reactions"] Difficulties --> WHO[Worse health outcomes] CC -- Yes --> Skills["Skills to function in health care system"] Skills --> BHO[Better health outcomes] </pre> <p>Ⓡ Ps82</p>
<p>Ps83</p>	<p>Cross-Cultural Research Competence</p>	<p>Culture - FGIDs Cross-Cultural Research Competence</p> <ul style="list-style-type: none"> • Consider differences in: <ul style="list-style-type: none"> • Symptom presentation • Health care seeking and utilization • Illness beliefs (explanatory models) • Psychosocial variables • Avoid ethnocentricity <ul style="list-style-type: none"> • Most studies focus on Caucasian populations from Western countries <p>Ⓡ Ps83</p>
<p>Ps84</p>	<p>Summary</p>	<p>Culture - FGIDs Summary</p> <ul style="list-style-type: none"> • Interactions between health and culture affect health care outcomes • Physicians should be conscious of patients' explanatory models and their level of health literacy • Physicians should develop cross-cultural competence • Appropriately conducted cross-cultural research can add to the understanding of FGID's <p>Ⓡ Ps84</p>

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Slide Number	Slide Title	Slide Image
T1	Multicomponent Approach to Functional GI Disorders-Slide 1 of 9	 <p>Multicomponent Approach to Functional GI Disorders</p> <ul style="list-style-type: none">• Establish therapeutic relationship <p>R T1</p>
T2	Establish Therapeutic Relationship	 <p>Establish Therapeutic Relationship</p> <ul style="list-style-type: none">• Introduction – establish personal connection• Provide adequate time now or in near future• Establish reason for the visit• Ask patient's principle concerns• Perform a thorough history and a directed physical examination <p>R T2</p>
T3	Multicomponent Approach to Functional GI Disorders-Slide 2 of 9	 <p>Multicomponent Approach to Functional GI Disorders</p> <ul style="list-style-type: none">• Establish therapeutic relationship• Assess patient's medical history, personality, and family <p>R T3</p>

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<p>T4</p>	<p>Assess Patient's Medical History, Psychosocial Situation, and Family</p>	<p>Assess Patient's Medical History, Psychosocial Situation, and Family</p> <ul style="list-style-type: none"> • Standard history <ul style="list-style-type: none"> • Look for FGID symptoms • Note any red flags • Take personal history: <ul style="list-style-type: none"> - relevant life events (abuse, loss, grief) - or psychological disturbance • Inquire about drugs / diet / lifestyle • Determine patient's expectations  <p>R T4</p>
<p>T5</p>	<p>Multicomponent Approach to Functional GI Disorders-Slide 3 of 9</p>	<p>Multicomponent Approach to Functional GI Disorders</p> <ul style="list-style-type: none"> • Establish therapeutic relationship • Assess patient's medical history, personality, and family • Assess quality of life and level of daily functioning <p>R T5</p>
<p>T6</p>	<p>Assess Quality of Life and Level of Daily Functioning</p>	<p>Assess Quality of Life and Level of Daily Functioning</p> <ul style="list-style-type: none"> • Do symptoms impair living by causing ... <ul style="list-style-type: none"> • Absenteeism/reduced productivity? • Sexual and physical dysfunction? • Impaired relationships? • Sadness, anger • Home confinement ? • Job and marital dissatisfaction ? • What aspect(s) of FGID most trouble the patient? <p>R T6</p>





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T7	Multicomponent Approach to Functional GI Disorders-Slide 4 of 9	<p>Multicomponent Approach to Functional GI Disorders</p> <ul style="list-style-type: none">• Establish therapeutic relationship• Assess patient's medical history, personality, and family• Assess quality of life and level of daily functioning• Take psychosocial history <p>RT T7</p>
T8	Assess Recent Life Stress and Psychological Distress or Any Precipitating Factors	<p>Assess Recent Life Stress and Psychological Distress or Any Precipitating Factors</p> <ul style="list-style-type: none">• Anxiety, depression or other• Recent life stress, abuse, or loss• Precipitating factors• Coping skills <p>RT T8</p>
T9	Multicomponent Approach to Functional GI Disorders-Slide 5 of 9	<p>Multicomponent Approach to Functional GI Disorders</p> <ul style="list-style-type: none">• Establish therapeutic relationship• Assess patient's medical history, personality, and family• Assess quality of life and level of daily functioning• Take psychosocial history• Order appropriate diagnostic testing <p>RT T9</p>




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T10	Review Appropriate Diagnostic Testing and Discuss Results	<p>Review Appropriate Diagnostic Testing and Discuss Results</p> <ul style="list-style-type: none">• Clear objectives guide the diagnostic plan• Use red flags to guide investigation• Thoroughly review results with patient• Address any concerns and questions• Explain that a negative test is good news <p>Ⓡ T10</p>
T11	Multicomponent Approach to Functional GI Disorders-Slide 6 of 9	<p>Multicomponent Approach to Functional GI Disorders</p> <ul style="list-style-type: none">• Establish therapeutic relationship• Assess patient's medical history, personality, and family• Assess quality of life and level of daily functioning• Take psychosocial history• Order appropriate diagnostic testing• Make a confident diagnosis <p>Ⓡ T11</p>
T12	Make A Confident Diagnosis	<p>Make A Confident Diagnosis</p> <ul style="list-style-type: none">• Use Rome III criteria as a guide• Note somatic and psychological comorbidities• Provide meaning and context for symptoms <p>Ⓡ T12</p>

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T13	Multicomponent Approach to Functional GI Disorders-Slide 7 of 9	<p>Multicomponent Approach to Functional GI Disorders</p> <ul style="list-style-type: none">• Establish therapeutic relationship• Assess patient's medical history, personality, and family• Assess quality of life and level of daily functioning• Take psychosocial history• Order appropriate diagnostic testing• Make a confident diagnosis• Explain and reassure <p> T13</p>
T14	Explain and Reassure	<p>Explain and Reassure</p> <ul style="list-style-type: none">• Encourage positive attitude, but realistic expectations• Discuss and reassure<ul style="list-style-type: none">• FGIDs are prevalent conditions• Benign clinical course• Intermittent symptoms likely• Variable impact on quality of life and impaired activities of daily living• Although "cure" unlikely, most patients improve with management <p></p> <p> T14</p>
T15	Multicomponent Approach to Functional GI Disorders-Slide 8 of 9	<p>Multicomponent Approach to Functional GI Disorders</p> <ul style="list-style-type: none">• Establish therapeutic relationship• Assess patient's medical history, personality, and family• Assess quality of life and level of daily functioning• Take psychosocial history• Order appropriate diagnostic testing• Make a confident diagnosis• Explain and reassure• Institute appropriate treatment <p> T15</p>

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T16	Institute Appropriate Treatment	<p>Institute Appropriate Treatment</p> <ul style="list-style-type: none">• Dietary advice• Lifestyle advice• Judicious drug treatment<ul style="list-style-type: none">• Many in primary care do not need drugs• Use when work or social function are impaired• Should be evidence-based• Target troublesome symptoms• Prescribe short-term or as needed• Encourage follow-up <p> T16</p>
T17	Multicomponent Approach to Functional GI Disorders: Summary Slide-Slide 9 of 9	<p>Multicomponent Approach to Functional GI Disorders</p> <ul style="list-style-type: none">• Establish therapeutic relationship• Assess patient's medical history, personality, and family• Assess quality of life and level of daily functioning• Take psychosocial history• Order appropriate diagnostic testing• Make a confident diagnosis• Explain and reassure• Institute appropriate treatment <p> T17</p>
T18	Suggested General Measures for Constipation	<p>Suggested General Measures for Constipation</p> <ul style="list-style-type: none">• Discontinue constipating medication/s• Correct endocrine diseases• Treat depression• Reassure• Regular visits to the toilet, increased fluid intake, and exercise <p> T18</p>

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<p>T19</p>	<p>Assess "Severity": Mild-Slide 1 of 4</p>	<p>Assess "Severity"</p> <ul style="list-style-type: none"> • What do symptoms mean? • Worried about cancer • What should be done? <p>Mild</p> <p>T19</p>
<p>T20</p>	<p>Assess "Severity": Moderate-Slide 2 of 4</p>	<p>Assess "Severity"</p> <ul style="list-style-type: none"> • Persistent symptoms and stress • Impairs QOL • Seeks relief of symptoms <p>+</p> <ul style="list-style-type: none"> • What do symptoms mean? • Worried about cancer • What should be done? <p>Moderate</p> <p>Mild</p> <p>T20</p>
<p>T21</p>	<p>Assess "Severity": Severe-Slide 3 of 4</p>	<p>Assess "Severity"</p> <ul style="list-style-type: none"> • Dependent and coping ineffectively • Impaired employment and social functioning • Physical and psychological comorbidity <p>+</p> <ul style="list-style-type: none"> • Persistent symptoms and stress • Impairs QOL • Seeks relief of symptoms <p>+</p> <ul style="list-style-type: none"> • What do symptoms mean? • Worried about cancer • What should be done? <p>Severe</p> <p>Moderate</p> <p>Mild</p> <p>T21</p>




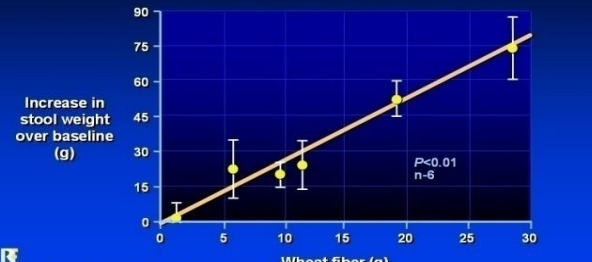
Computer-Based Learning Program
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<p>T22</p>	<p>Assess "Severity": Mild, Moderate, Severe-Slide 4 of 4</p>	<p>Assess "Severity"</p> <ul style="list-style-type: none"> • Dependent and coping ineffectively • Impaired employment and social functioning • Physical and psychological comorbidity <ul style="list-style-type: none"> • Persistent symptoms and stress • Impairs QOL • Seeks relief of symptoms <ul style="list-style-type: none"> • What do symptoms mean? • Worried about cancer • What should be done? <p>T22</p>
<p>T23</p>	<p>Graded Treatment-Slide 1 of 4</p>	<p>Graded Treatment Response</p> <ul style="list-style-type: none"> • Diet, lifestyle advice • Positive diagnosis • Explain, reassure <p>T23</p>
<p>T24</p>	<p>Graded Treatment Response-Slide 2 of 4</p>	<p>Graded Treatment Response</p> <ul style="list-style-type: none"> • Follow-up visit • Manage stress • Pharmacotherapy <p>T24</p>

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<p>T25</p>	<p>Graded Treatment Response-Slide 3 of 4</p>	
<p>T26</p>	<p>Graded Treatment Response-Slide 4 of 4</p>	
<p>T27</p>	<p>Dietary Advice for IBS</p>	


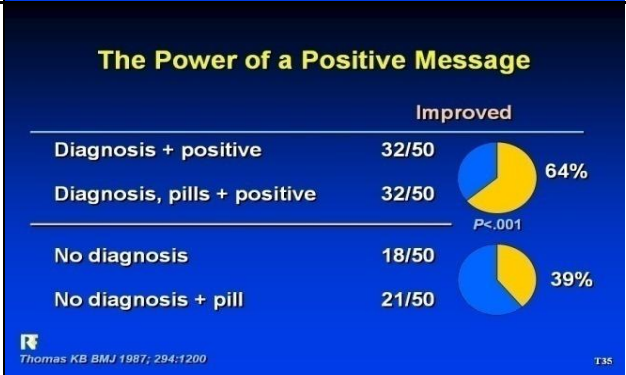
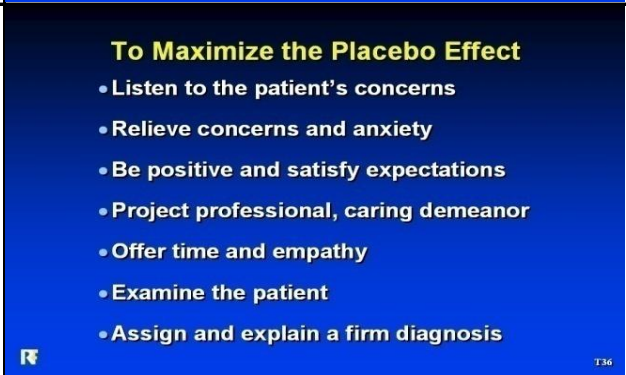
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<p>T28</p>	<p>Food: The forgotten Factor</p>	<p>Food: The Forgotten Factor</p> <p>Up to 2/3 of IBS patients associate symptoms with eating a meal</p>  <p>Food intolerances Gastrocolonic response</p> <p>Psychological factors Gas handling Fermentation</p> <p><small>Smiren M et al. Clin Gastroenterol Hepatol 2007; 5:201</small></p>
<p>T29</p>	<p>Dietary Advice</p>	<p>Dietary Advice</p> <ul style="list-style-type: none"> • No standard FGID diet! • Avoid excess <ul style="list-style-type: none"> • Caffeine, chocolate, alcohol • Antidiarrheals • Sorbitol • Fatty or junk food • Encourage <ul style="list-style-type: none"> • Dietary fiber for hard stools • Antireflux measures for heartburn • Allow sufficient time and quiet for meals   <p><small>Stephen AM et al. Br J Nutrition 1986; 56:349</small></p>
<p>T30</p>	<p>Wheat Bran and Stool Weight: A Dose Response</p>	<p>Wheat Bran and Stool Weight: A Dose Response</p>  <p>Increase in stool weight over baseline (g)</p> <p>Wheat fiber (g)</p> <p>$P < 0.01$ $n = 6$</p> <p><small>Stephen AM et al. Br J Nutrition 1986; 56:349</small></p>

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<p>T31</p>	<p>Placebos in Clinical Trials</p>	<p>Placebos in Clinical Trials</p> <ul style="list-style-type: none"> • An intervention that controls for the active treatment in a clinical trial and is believed to lack any specific effect on the disorder • Placebo response rate <ul style="list-style-type: none"> • 10% to 70% for functional dyspepsia¹ • 0% to 84% for IBS² • Placebo response is influenced by parallel interventions, natural improvement (regression to the mean) + the placebo effect. <p><small>¹Veldhuyzen van Zanten SJ et al. Am J Gastroenterol 1996; 91:660 ²Spiller RC. Am J Med 1999; 107:91S</small></p> <p>T31</p>
<p>T32</p>	<p>Components of a Therapeutic Outcome-Slide 1 of 2</p>	<p>Components of a Therapeutic Outcome</p> <p>The graph plots '% with relief' on the y-axis (0 to 60) against 'Week' on the x-axis (0 to 16). The 'Drug arm' (solid line) starts at ~35% at week 0, rises to ~50% by week 2, and remains relatively stable around 45-50% until week 12. The 'Placebo arm' (dotted line) starts at ~35% at week 0, rises to ~45% by week 2, and remains stable around 40-45% until week 12. After week 12, both arms drop, but the Placebo arm drops more sharply to ~25% by week 16. A shaded yellow area between the two lines from week 2 to week 12 is labeled 'Therapeutic gain'. A vertical line at week 12 separates the 'Treatment period' from the 'Follow-up period'. A note '* P < 0.05' is present in the follow-up period.</p> <p>T32</p>
<p>T33</p>	<p>Without Placebo and Time Effects . . .-Slide 2 of 2</p>	<p>Without Placebo and Time Effects . . .</p> <p>The graph plots '% with relief' on the y-axis (0 to 60) against 'Week' on the x-axis (0 to 16). The 'Placebo arm' (dotted line) starts at ~35% at week 0, rises to ~45% by week 2, and remains stable around 40-45% until week 12. The 'Drug arm' (solid line) starts at ~10% at week 0, rises to ~15% by week 2, and remains stable around 10-15% until week 12. After week 12, both arms drop, but the Drug arm drops more sharply to ~5% by week 16. A vertical line at week 12 separates the 'Treatment period' from the 'Follow-up period'. A note '* P < 0.05' is present in the follow-up period.</p> <p>T33</p>


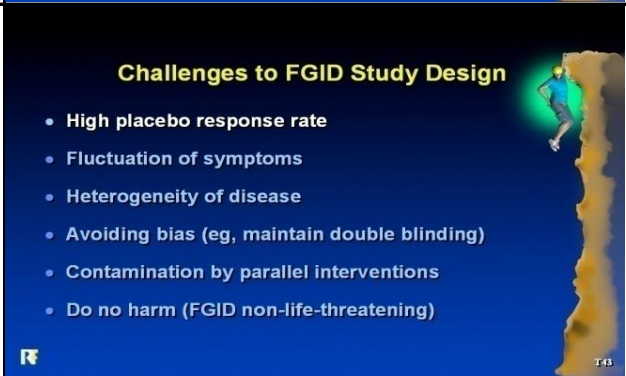
Computer-Based Learning Program
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<p>T34</p>	<p>The Power of a Positive Message-Slide 1 of 2</p>	 <p>The Power of a Positive Message</p> <table border="1"> <thead> <tr> <th>N</th> <th>Diagnosis</th> <th>Doctor Attitude</th> </tr> </thead> <tbody> <tr> <td>50</td> <td>Yes</td> <td>‘You will be better soon.’</td> </tr> <tr> <td>50</td> <td>Yes + pills</td> <td>“Pills will help.”</td> </tr> <tr> <td>50</td> <td>No</td> <td>“I don’t know what . . .”</td> </tr> <tr> <td>50</td> <td>No + pills</td> <td>“I don’t know if . . .”</td> </tr> </tbody> </table> <p>200 GP Patients with Indefinite Diagnosis Thomas KB BMJ 1987; 294:1200</p> <p>T34</p>	N	Diagnosis	Doctor Attitude	50	Yes	‘You will be better soon.’	50	Yes + pills	“Pills will help.”	50	No	“I don’t know what . . .”	50	No + pills	“I don’t know if . . .”
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<p>T35</p>	<p>The Power of a Positive Message-Slide 2 of 2</p>	 <p>The Power of a Positive Message</p> <table border="1"> <thead> <tr> <th>Group</th> <th>Improved</th> <th>Percentage</th> </tr> </thead> <tbody> <tr> <td>Diagnosis + positive</td> <td>32/50</td> <td>64%</td> </tr> <tr> <td>Diagnosis, pills + positive</td> <td>32/50</td> <td>64%</td> </tr> <tr> <td>No diagnosis</td> <td>18/50</td> <td>39%</td> </tr> <tr> <td>No diagnosis + pill</td> <td>21/50</td> <td>39%</td> </tr> </tbody> </table> <p><i>P</i> < .001</p> <p>Thomas KB BMJ 1987; 294:1200</p> <p>T35</p>	Group	Improved	Percentage	Diagnosis + positive	32/50	64%	Diagnosis, pills + positive	32/50	64%	No diagnosis	18/50	39%	No diagnosis + pill	21/50	39%
Group	Improved	Percentage															
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Diagnosis, pills + positive	32/50	64%															
No diagnosis	18/50	39%															
No diagnosis + pill	21/50	39%															
<p>T36</p>	<p>To Maximize the Placebo Effect</p>	 <p>To Maximize the Placebo Effect</p> <ul style="list-style-type: none"> • Listen to the patient’s concerns • Relieve concerns and anxiety • Be positive and satisfy expectations • Project professional, caring demeanor • Offer time and empathy • Examine the patient • Assign and explain a firm diagnosis <p>Thomas KB BMJ 1987; 294:1200</p> <p>T36</p>															
<p>T37</p>	<p>Section Title-Design of Treatment Trials</p>	<p></p>															

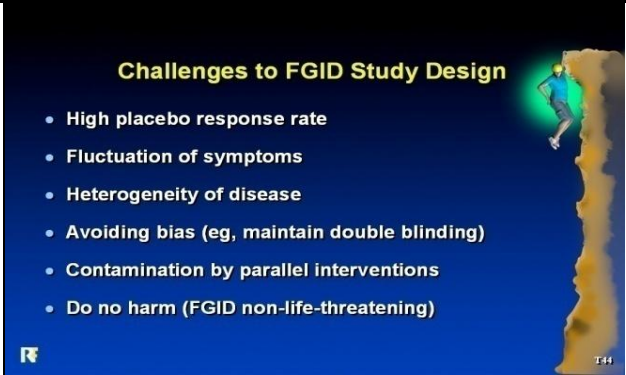
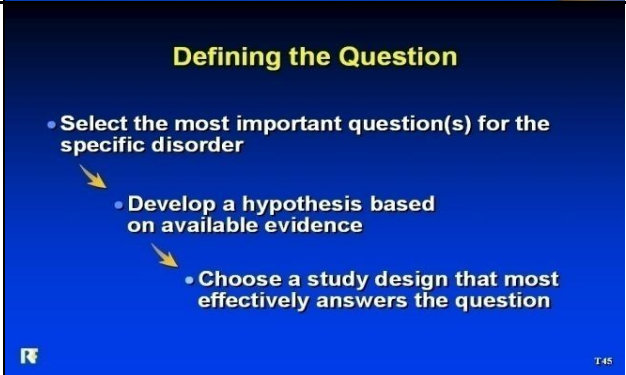
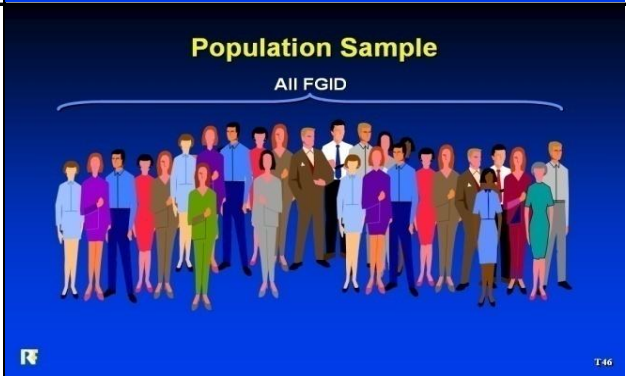
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T38	Challenges to FGID Study Design-Slide 1 of 7	 <p>Challenges to FGID Study Design</p> <ul style="list-style-type: none">• Do no harm (FGID non-life-threatening) <p>© T38</p>
T39	Challenges to FGID Study Design-Slide 2 of 7	 <p>Challenges to FGID Study Design</p> <ul style="list-style-type: none">• Contamination by parallel interventions• Do no harm (FGID non-life-threatening) <p>© T39</p>
T40	Challenges to FGID Study Design-Slide 3 of 7	 <p>Challenges to FGID Study Design</p> <ul style="list-style-type: none">• Avoiding bias (eg, maintain double blinding)• Contamination by parallel interventions• Do no harm (FGID non-life-threatening) <p>© T40</p>

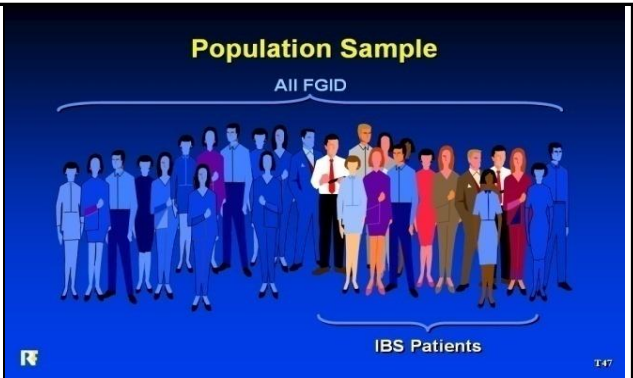
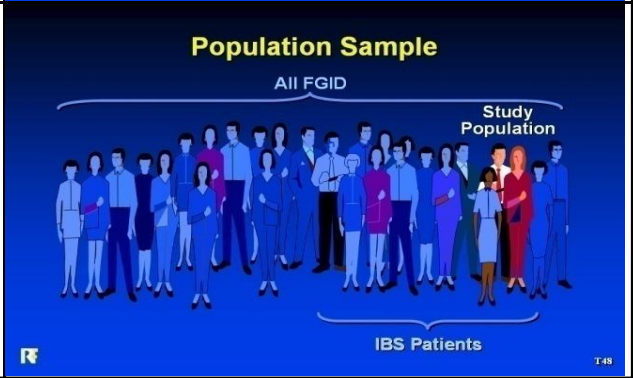
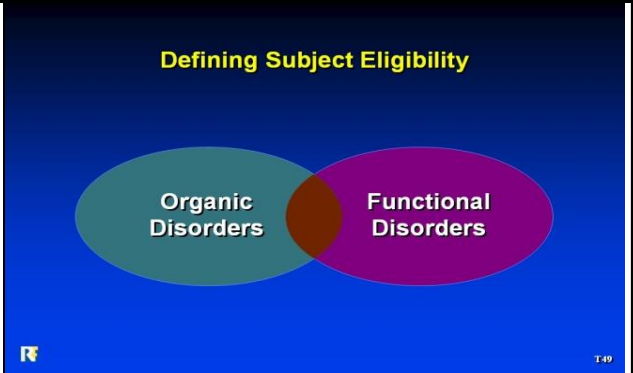
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T41	Challenges to FGID Study Design-Slide 4 of 7	 <p>Challenges to FGID Study Design</p> <ul style="list-style-type: none">• Multifactorial mechanisms• Avoiding bias (eg, maintain double blinding)• Contamination by parallel interventions• Do no harm (FGID non-life-threatening) <p>T41</p>
T42	Challenges to FGID Study Design-Slide 5 of 7	 <p>Challenges to FGID Study Design</p> <ul style="list-style-type: none">• Fluctuation of symptoms• Multifactorial mechanisms• Avoiding bias (eg, maintain double blinding)• Contamination by parallel interventions• Do no harm (FGID non-life-threatening) <p>T42</p>
T43	Challenges to FGID Study Design-Slide 6 of 7	 <p>Challenges to FGID Study Design</p> <ul style="list-style-type: none">• High placebo response rate• Fluctuation of symptoms• Heterogeneity of disease• Avoiding bias (eg, maintain double blinding)• Contamination by parallel interventions• Do no harm (FGID non-life-threatening) <p>T43</p>

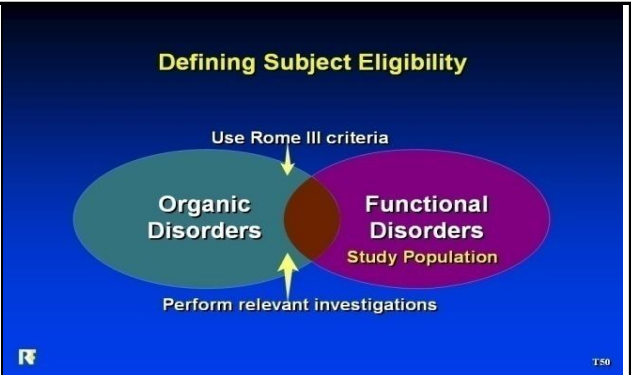
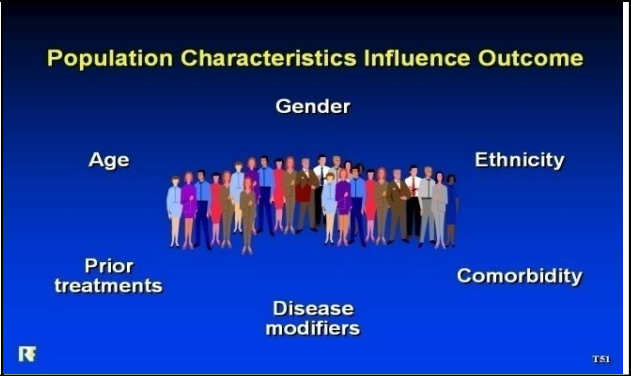
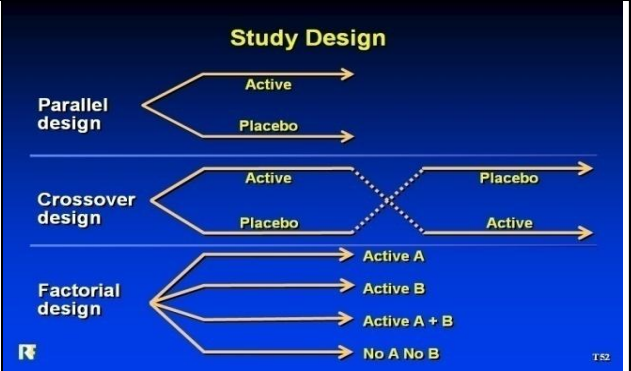
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T44	Challenges to FGID Study Design-Slide 7 of 7	 <p>Challenges to FGID Study Design</p> <ul style="list-style-type: none">• High placebo response rate• Fluctuation of symptoms• Heterogeneity of disease• Avoiding bias (eg, maintain double blinding)• Contamination by parallel interventions• Do no harm (FGID non-life-threatening) <p>RE T44</p>
T45	Defining the Question for a Treatment Trial	 <p>Defining the Question</p> <ul style="list-style-type: none">• Select the most important question(s) for the specific disorder<ul style="list-style-type: none">• Develop a hypothesis based on available evidence• Choose a study design that most effectively answers the question <p>RE T45</p>
T46	Population Sample-Slide 1 of 3	 <p>Population Sample</p> <p>All FGID</p> <p>RE T46</p>

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T47	Population Sample-Slide 2 of 3	 <p>Population Sample All FGID IBS Patients</p>
T48	Population Sample-Slide 3 of 3	 <p>Population Sample All FGID Study Population IBS Patients</p>
T49	Defining Subject Eligibility-Slide 1 of 2	 <p>Defining Subject Eligibility Organic Disorders Functional Disorders</p>

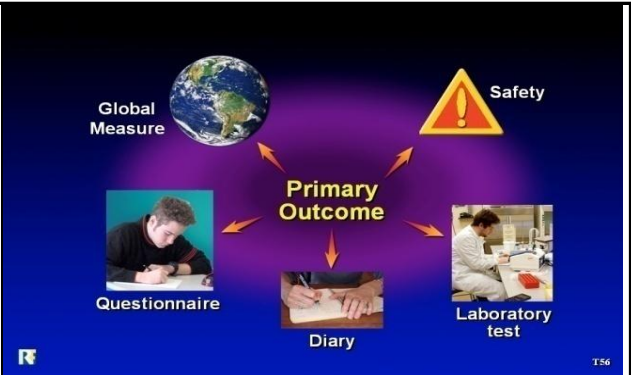
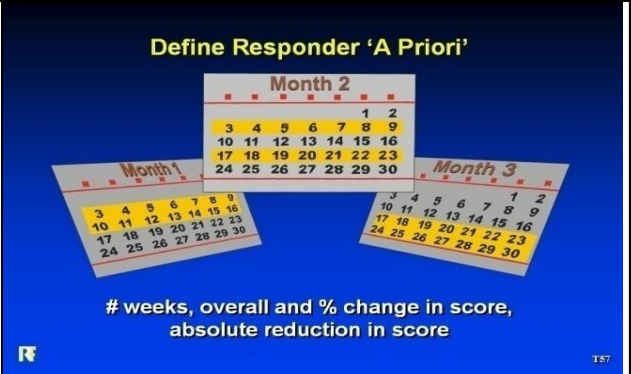
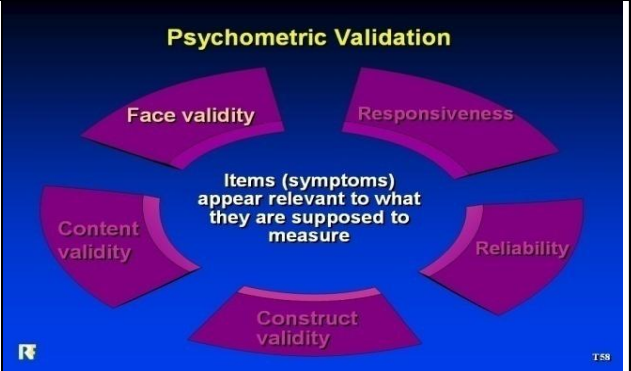
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T50	Defining Subject Eligibility-Slide 2 of 2	 <p>Defining Subject Eligibility</p> <p>Use Rome III criteria</p> <p>Organic Disorders</p> <p>Functional Disorders Study Population</p> <p>Perform relevant investigations</p> <p>T50</p>
T51	Population Characteristics Influence Outcome	 <p>Population Characteristics Influence Outcome</p> <p>Gender</p> <p>Age</p> <p>Ethnicity</p> <p>Prior treatments</p> <p>Disease modifiers</p> <p>Comorbidity</p> <p>T51</p>
T52	Study Design	 <p>Study Design</p> <p>Parallel design</p> <p>Active</p> <p>Placebo</p> <p>Crossover design</p> <p>Active</p> <p>Placebo</p> <p>Placebo</p> <p>Active</p> <p>Factorial design</p> <p>Active A</p> <p>Active B</p> <p>Active A + B</p> <p>No A No B</p> <p>T52</p>

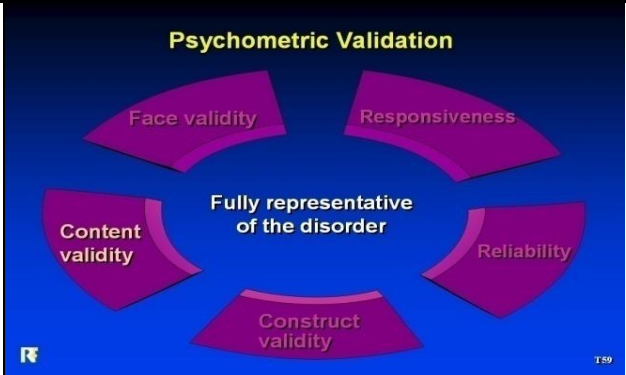
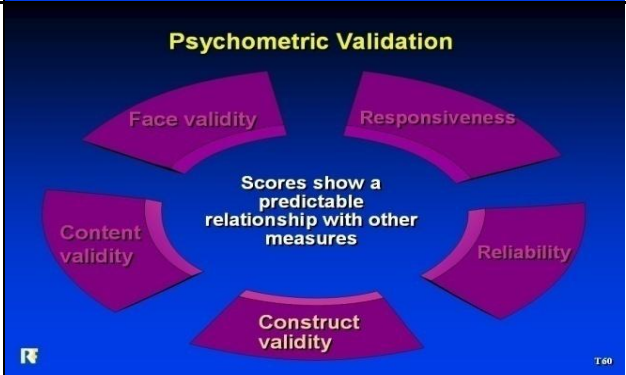
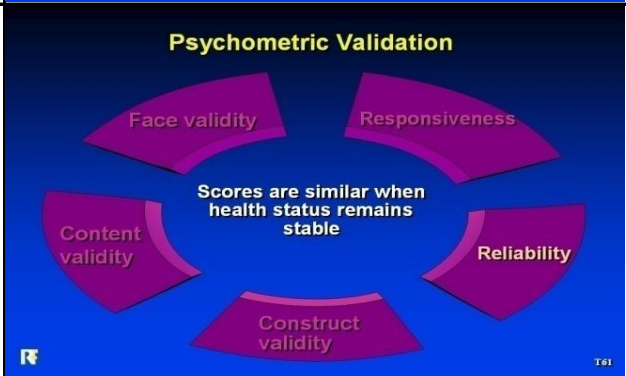
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T53	Maximizing Blinding	<p>Maximizing Blinding</p>  <p>Statistician or data manager</p> <p>Investigator</p> <p>Single, Double, Triple-Blinding</p> <p>Patient</p> <p>T53</p>
T54	Minimize Bias	<p>Minimize Bias</p>  <p>Systematic error</p> <p>No bias or error</p> <p>Objective outcome assessments</p> <ul style="list-style-type: none">• Questionnaire, lab test, diary• Independent assessor <p>T54</p>
T55	Outcome Assessment	<p>Outcome Assessment</p>  <ul style="list-style-type: none">• One (or two) primary outcomes• Secondary measures• Use validated instruments• Define “responder” a priori• Translate results to clinical realm <p>T55</p>

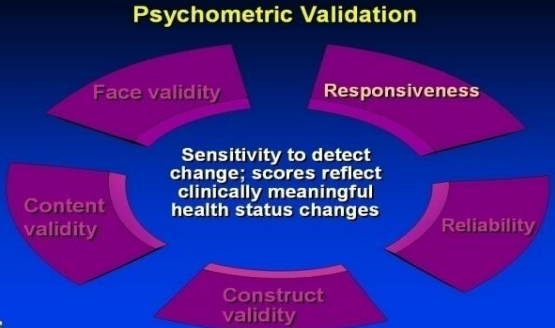
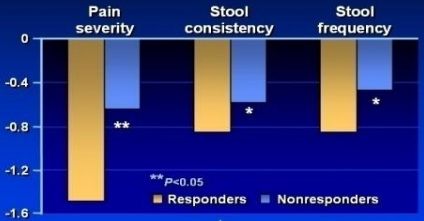
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<p>T56</p>	<p>Primary Outcome</p>	 <p>Global Measure</p> <p>Safety</p> <p>Primary Outcome</p> <p>Questionnaire</p> <p>Diary</p> <p>Laboratory test</p> <p>T56</p>
<p>T57</p>	<p>Define Responder 'A Priori'</p>	 <p>Define Responder 'A Priori'</p> <p>Month 1</p> <p>Month 2</p> <p>Month 3</p> <p># weeks, overall and % change in score, absolute reduction in score</p> <p>T57</p>
<p>T58</p>	<p>Psychometric Validation: Face Validity</p>	 <p>Psychometric Validation</p> <p>Face validity</p> <p>Responsiveness</p> <p>Reliability</p> <p>Construct validity</p> <p>Content validity</p> <p>Items (symptoms) appear relevant to what they are supposed to measure</p> <p>T58</p>

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T59	Psychometric Validation: Content Validity	 <p>Psychometric Validation</p> <p>Face validity Responsiveness</p> <p>Content validity Fully representative of the disorder Reliability</p> <p>Construct validity</p> <p><small>© T59</small></p>
T60	Psychometric Validation: Construct Validity	 <p>Psychometric Validation</p> <p>Face validity Responsiveness</p> <p>Content validity Scores show a predictable relationship with other measures Reliability</p> <p>Construct validity</p> <p><small>© T60</small></p>
T61	Psychometric Validation: Reliability	 <p>Psychometric Validation</p> <p>Face validity Responsiveness</p> <p>Content validity Scores are similar when health status remains stable Reliability</p> <p>Construct validity</p> <p><small>© T61</small></p>

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<p>T62</p>	<p>Psychometric Validation: Responsiveness</p>	<p>Psychometric Validation</p>  <p>Face validity</p> <p>Responsiveness</p> <p>Reliability</p> <p>Construct validity</p> <p>Content validity</p> <p>Sensitivity to detect change; scores reflect clinically meaningful health status changes</p> <p><small>T62</small></p>												
<p>T63</p>	<p>Adequate Relief</p>	<p>Adequate Relief</p> <ul style="list-style-type: none"> • Yes or No: In the past 7 days have you had <i>adequate relief</i> of your irritable bowel syndrome pain and discomfort? • Measured weekly over 12 weeks • RESPONDER: answered 'yes' for 2/4 weeks each month <p><small>Mangel AW et al. J Int Med Res 1998; 26:76</small></p> <p><small>T63</small></p>												
<p>T64</p>	<p>Improved Pain and Stool Parameters in Alosetron Responders with "Adequate Relief"</p>	<p>Improved Pain and Stool Parameters in Alosetron Responders with "Adequate Relief"</p>  <table border="1"> <caption>Approximate data from the bar chart</caption> <thead> <tr> <th>Parameter</th> <th>Responders (Change)</th> <th>Nonresponders (Change)</th> </tr> </thead> <tbody> <tr> <td>Pain severity</td> <td>-1.4</td> <td>-0.6</td> </tr> <tr> <td>Stool consistency</td> <td>-0.8</td> <td>-0.4</td> </tr> <tr> <td>Stool frequency</td> <td>-1.0</td> <td>-0.5</td> </tr> </tbody> </table> <p>** p<0.05</p> <p>* Correlations and reliability were not reported</p> <p><small>Mangel AW et al. J Int Med Res 1998; 26:76</small></p> <p><small>T64</small></p>	Parameter	Responders (Change)	Nonresponders (Change)	Pain severity	-1.4	-0.6	Stool consistency	-0.8	-0.4	Stool frequency	-1.0	-0.5
Parameter	Responders (Change)	Nonresponders (Change)												
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<p>T65</p>	<p>Improved IBSQOL Quality of Life Scores in Alosetron Responders With “Adequate Relief”</p>	<p>Improved IBSQOL Quality of Life Scores in Alosetron Responders With “Adequate Relief”</p> <table border="1"> <caption>Approximate IBSQOL Scores from Graph</caption> <thead> <tr> <th>Domain</th> <th>Responders</th> <th>Nonresponders</th> </tr> </thead> <tbody> <tr> <td>Emotional</td> <td>38</td> <td>25</td> </tr> <tr> <td>Mental health</td> <td>25</td> <td>18</td> </tr> <tr> <td>Sleep</td> <td>28</td> <td>20</td> </tr> <tr> <td>Energy</td> <td>45</td> <td>30</td> </tr> <tr> <td>Physical function</td> <td>28</td> <td>18</td> </tr> <tr> <td>Food</td> <td>32</td> <td>22</td> </tr> <tr> <td>Social</td> <td>40</td> <td>28</td> </tr> <tr> <td>Role physical</td> <td>45</td> <td>30</td> </tr> <tr> <td>Sexual function</td> <td>28</td> <td>18</td> </tr> </tbody> </table> <p><i>Mangel AW et al. J Int Med Res 1998; 26:76</i></p>	Domain	Responders	Nonresponders	Emotional	38	25	Mental health	25	18	Sleep	28	20	Energy	45	30	Physical function	28	18	Food	32	22	Social	40	28	Role physical	45	30	Sexual function	28	18
Domain	Responders	Nonresponders																														
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Sleep	28	20																														
Energy	45	30																														
Physical function	28	18																														
Food	32	22																														
Social	40	28																														
Role physical	45	30																														
Sexual function	28	18																														
<p>T66</p>	<p>Satisfactory Relief</p>	<p>Satisfactory Relief</p> <ul style="list-style-type: none"> • Over the past week do you consider that you have had satisfactory relief of your IBS symptoms? • Measured weekly over 12 weeks • RESPONDER: answered ‘yes’ to 50% of weeks • Validation: global relief (5-point scale); 100-mm VAS, stool frequency, stool consistency, pain severity, bloating severity, use of laxatives. <p><i>Muller-Lissner SA et al. J. Clin Epidemiol 2003; 56: 310-16</i></p>																														
<p>T67</p>	<p>Number of Symptoms Improved With Subjective Global Assessment (SGA) of Relief</p>	<p>Number of Symptoms Improved With Subjective Global Assessment (SGA) of Relief</p> <table border="1"> <thead> <tr> <th>Group</th> <th>Number of symptoms improved</th> </tr> </thead> <tbody> <tr> <td>Responders</td> <td>5</td> </tr> <tr> <td>Non-responders</td> <td>2*</td> </tr> </tbody> </table> <p><i>Muller-Lissner SA et al. Aliment Pharmacol Ther 2001; 15:1655</i></p>	Group	Number of symptoms improved	Responders	5	Non-responders	2*																								
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<p>T68</p>	<p>Mean Symptom Score Changes in Responders Reporting Satisfactory Relief</p>	<p>Mean Symptom Score Changes in Responders Reporting Satisfactory Relief</p> <table border="1"> <thead> <tr> <th>Symptom</th> <th>Responders</th> <th>Nonresponders</th> </tr> </thead> <tbody> <tr> <td>Pain</td> <td>~ -50</td> <td>~ -10</td> </tr> <tr> <td>Bloating</td> <td>~ -40</td> <td>~ -10</td> </tr> <tr> <td>Days no BM</td> <td>~ -45</td> <td>~ -15</td> </tr> </tbody> </table> <p><i>Muller-Lissner SA et al. Aliment Pharmacol Ther 2001;15:1655</i></p>	Symptom	Responders	Nonresponders	Pain	~ -50	~ -10	Bloating	~ -40	~ -10	Days no BM	~ -45	~ -15
Symptom	Responders	Nonresponders												
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<p>T69</p>	<p>Adequate and Satisfactory Relief</p>	<p>Adequate and Satisfactory Relief</p> <table border="1"> <thead> <tr> <th>Pros</th> <th>Cons</th> </tr> </thead> <tbody> <tr> <td> <ul style="list-style-type: none"> • Enables comparison across trials • Enables pooling of results • Assesses patient preferences </td> <td> <ul style="list-style-type: none"> • Composite questions • Some symptoms improve, others worsen • Not fully validated against other measures </td> </tr> </tbody> </table>	Pros	Cons	<ul style="list-style-type: none"> • Enables comparison across trials • Enables pooling of results • Assesses patient preferences 	<ul style="list-style-type: none"> • Composite questions • Some symptoms improve, others worsen • Not fully validated against other measures 								
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<p>T70</p>	<p>Secondary Outcome</p>	<p>Secondary Outcome</p> <ul style="list-style-type: none"> Questionnaire Disability Diary Laboratory test <p>Individual symptoms 1 2 3 4 5 Good Bad Likert scale</p>												

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T71	Scales for Primary or Secondary Outcomes: Combined Scale-Slide 1 of 4	<p>Scales for Primary or Secondary Outcomes: Combined Scale</p> <p>Step one: Are you better, the same or worse?</p>  <p>T71</p>
T72	Scales for Primary or Secondary Outcomes: Combined Scale-Slide 2 of 4	<p>Scales for Primary or Secondary Outcomes: Combined Scale</p> <p>Step two: Are you?</p>  <ul style="list-style-type: none">+3 Markedly better+2 Somewhat better+1 A little better <p>T72</p>
T73	Scales for Primary or Secondary Outcomes: Combined Scale-Slide 3 of 4	<p>Scales for Primary or Secondary Outcomes: Combined Scale</p> <p>Step two: Are you?</p>  <ul style="list-style-type: none">-1 A little worse-2 Somewhat worse-3 Markedly worse <p>T73</p>

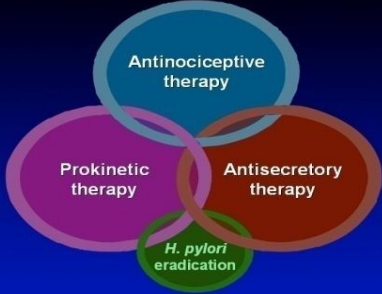

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<p>T74</p>	<p>Scales for Primary or Secondary Outcomes: Combined Scale-Slide 4 of 4</p>	<p>Scales for Primary or Secondary Outcomes: Combined Scale</p> <p>Step one: Are you?</p>  <ul style="list-style-type: none"> +3 Markedly better +2 Somewhat better +1 A little better 0 The same -1 A little worse -2 Somewhat worse -3 Markedly worse <p><small>T74</small></p>													
<p>T75</p>	<p>Statistical Analysis: Sample Size</p>	<p>Statistical Analysis: Sample Size</p> <table border="1"> <thead> <tr> <th colspan="2" rowspan="2"></th> <th colspan="2"><i>Truth</i></th> </tr> <tr> <th>Experimental Rx is superior</th> <th>Experimental Rx is not superior</th> </tr> </thead> <tbody> <tr> <th rowspan="2"><i>Trial results</i></th> <th>Experimental Rx appears superior</th> <td>Power = $1 - \beta$ <i>Accurate result</i></td> <td>Type I error <i>Risk = α</i> <i>(P value)</i></td> </tr> <tr> <th>Experimental Rx appears not superior</th> <td>Type II error <i>Risk = β</i></td> <td>Accurate result <i>Prob = $1 - \alpha$</i></td> </tr> </tbody> </table> <p><small>Convention set $\alpha = .05$; $\beta = .10$ or 0.2 ($1 - \text{Power}$)</small></p> <p><small>T75</small></p>			<i>Truth</i>		Experimental Rx is superior	Experimental Rx is not superior	<i>Trial results</i>	Experimental Rx appears superior	Power = $1 - \beta$ <i>Accurate result</i>	Type I error <i>Risk = α</i> <i>(P value)</i>	Experimental Rx appears not superior	Type II error <i>Risk = β</i>	Accurate result <i>Prob = $1 - \alpha$</i>
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<p>T76</p>	<p>Main Data Analysis</p>	<p>Main Data Analysis</p> <ul style="list-style-type: none"> • Adhere to CONSORT Guidelines www.consort-statement.org • Intention to Treat (ITT) is mandatory <ul style="list-style-type: none"> • Based on primary outcome(s) • Calculate NNT • Report actual 'P' values • Should report harms data • Use appropriate statistical methods for data <ul style="list-style-type: none"> • Adjust for multiple variables or important covariates <p><small>Altman DG et al. Ann Intern Med 2001; 134:663 Moher D et al. JAMA 2001; 285:1987</small></p> <p><small>T76</small></p>													

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<p>T77</p>	<p>The Consort E-Flowchart-August 2005</p>	<p>The Consort E-Flowchart – August, 2005</p> <p>Accessed for eligibility (n=)</p> <p>Enrollment Is it recommended?</p> <p>Excluded (n=) Not meeting inclusion criteria (n=) Refused to participate (n=) Other reasons (n=)</p> <p>Allocation</p> <p>Allocated to intervention (n=) Received allocated intervention (n=) Allocated interventions not received (n=) Give reasons</p> <p>Follow-up</p> <p>Lost to follow-up (n=) Give reasons Discontinued intervention (n=) Give reasons</p> <p>Analysis</p> <p>Analyzed (n=) Excluded from analysis (n=) Give reasons</p> <p>www.consort-statement.org</p> <p>T77</p>
<p>T78</p>	<p>Ethics and Reporting</p>	<p>Ethics and Reporting</p> <ul style="list-style-type: none"> • All randomized trials should be registered • Adherence to protocol and outcomes is vital <ul style="list-style-type: none"> • Consider independent advisory/safety monitoring board • Interpret the data objectively • Results of registered trials should be reported, irrespective of findings. <p>Irvine EJ et al. Gastroenterology 2006; 130:1538</p> <p>T78</p>
<p>T79</p>	<p>Section Title: Functional Dyspepsia</p>	
<p>T80</p>	<p>Dietary Recommendations for Functional Dyspepsia: What's the Evidence?</p>	<p>Dietary Recommendations for Functional Dyspepsia: What's the Evidence?</p> <ul style="list-style-type: none"> • Efficacy of dietary interventions has not been carefully studied in functional dyspepsia • Smaller meals may better tolerated <ul style="list-style-type: none"> • Patients develop fullness and other symptoms with smaller volumes of a nutrient drink or water vs controls • Avoid high-fat meals <ul style="list-style-type: none"> • Ingestion of fat or intraduodenal lipid infusion leads to more symptoms in patients vs controls <p>Felnie-Bisset C and Horowitz M. Neurogastroenterol Motil 2006; 18:608</p> <p>T80</p>

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<p>T81</p>	<p>Current Management of Functional Dyspepsia</p>	<p>Current Management of Functional Dyspepsia</p>  <p>T81</p>															
<p>T82</p>	<p>Cochrane Collaboration Meta-Analysis of <i>H. pylori</i> Cure for FD</p>	<p>Cochrane Collaboration Meta-Analysis of <i>H. pylori</i> Cure for FD</p> <ul style="list-style-type: none"> • 17 RCTs (3566 patients) • <i>H. pylori</i> eradication therapy vs placebo or short course of PPI <table border="1" data-bbox="1354 673 1906 836"> <thead> <tr> <th></th> <th>% Symptom Improvement (range)</th> <th>Therapeutic Gain (%)</th> <th>NNT (95% CI)</th> <th>RRR (%)</th> </tr> </thead> <tbody> <tr> <td><i>H. pylori</i> Cure</td> <td>36 (15-75)</td> <td>7</td> <td>14 (10-25)</td> <td>10 (6-14)</td> </tr> <tr> <td>Placebo</td> <td>29 (7-51)</td> <td></td> <td></td> <td></td> </tr> </tbody> </table> <p>Moayyedi P et al. Cochrane Database, 2006</p> <p>12/17 trials did not show significant benefits with <i>H. pylori</i> eradication</p> <p>T82</p>		% Symptom Improvement (range)	Therapeutic Gain (%)	NNT (95% CI)	RRR (%)	<i>H. pylori</i> Cure	36 (15-75)	7	14 (10-25)	10 (6-14)	Placebo	29 (7-51)			
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<p>T83</p>	<p>The Rationale for Antisecretory Therapy in Functional Dyspepsia</p>	<p>The Rationale for Antisecretory Therapy in Functional Dyspepsia</p> <ul style="list-style-type: none"> • Gastric acid secretion in FD similar to controls¹ • Acid hypersensitivity <ul style="list-style-type: none"> • Lowered threshold of mechanosensitive afferents² • Increased nausea with duodenal acid infusion³ • Increased duodenal acid exposure^{3,4} <ul style="list-style-type: none"> • Decreased fasting clearance of exogenous acid • Decreased fasting duodenal motor activity • Overlap of GERD and dyspeptic symptoms⁵ <ul style="list-style-type: none"> • Patients with GERD often have dyspeptic symptoms  <p>¹Bechi et al. Dig Dis Sci 1992; 37:378 ²Coffin et al. Am J Physiol 2001; 280:G904 ³Sansom et al. Gastroenterol 1999; 116:515 ⁴Lee et al. Am J Gastro 2004; 99:1765 ⁵Tack et al. Gut 2005; 54:1370</p> <p>T83</p>															

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<p>T84</p>	<p>Meta-Analysis of PPI Therapy for Functional Dyspepsia</p>	<p>Meta-Analysis of PPI Therapy for Functional Dyspepsia</p> <ul style="list-style-type: none"> • 10 RCTs (3347 patients) • PPI for 2-8 weeks was superior to placebo in relieving FD symptoms <table border="1"> <thead> <tr> <th></th> <th>% No or Minimal Symptoms</th> <th>Therapeutic Gain (%)</th> <th>NNT (95% CI)</th> <th>RRR (%) (95% CI)</th> </tr> </thead> <tbody> <tr> <td>PPI</td> <td>34</td> <td>9</td> <td>10 (7-33)</td> <td>13 (4-20)</td> </tr> <tr> <td>Placebo</td> <td>25</td> <td></td> <td></td> <td></td> </tr> </tbody> </table> <p><small>Moayyedi P et al. Cochrane Database 2006</small> <small>No asymmetry by funnel plot</small></p>		% No or Minimal Symptoms	Therapeutic Gain (%)	NNT (95% CI)	RRR (%) (95% CI)	PPI	34	9	10 (7-33)	13 (4-20)	Placebo	25								
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<p>T85</p>	<p>Efficacy of PPI Therapy in Functional Dyspepsia Subgroups</p>	<p>Efficacy of PPI Therapy in Functional Dyspepsia Subgroups</p> <table border="1"> <thead> <tr> <th>Predominant symptom</th> <th>RR</th> <th>95% CI</th> <th>Total</th> </tr> </thead> <tbody> <tr> <td>Dysmotility (5)</td> <td>1.02</td> <td>0.91 1.13</td> <td>683</td> </tr> <tr> <td>Epigastric (6)</td> <td>0.85</td> <td>0.79 0.92</td> <td>1384</td> </tr> <tr> <td>Reflux (6)</td> <td>0.75</td> <td>0.65 0.87</td> <td>415</td> </tr> <tr> <td>Combined (17)</td> <td>0.88</td> <td>0.83 0.93</td> <td>2492</td> </tr> </tbody> </table> <p><small>Nausea² and bloating³ are negative predictors of PPI response</small></p> <p><small>¹Moayyedi P et al. Cochrane Database 2006 ²Melnche-Schmidt V and Christensen E. Am J Gastroenterol 2000; 95:2777 ³Bolling-Sternevald E et al. Aliment Pharm Ther 2003; 18:117</small></p>	Predominant symptom	RR	95% CI	Total	Dysmotility (5)	1.02	0.91 1.13	683	Epigastric (6)	0.85	0.79 0.92	1384	Reflux (6)	0.75	0.65 0.87	415	Combined (17)	0.88	0.83 0.93	2492
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<p>T86</p>	<p>Meta-Analysis of H₂RA therapy for Functional Dyspepsia</p>	<p>Meta-Analysis of H₂RA therapy for Functional Dyspepsia</p> <ul style="list-style-type: none"> • 12 RCTs (2183 patients) <table border="1"> <thead> <tr> <th></th> <th>% No or Minimal Symptoms</th> <th>Therapeutic Gain (%)</th> <th>NNT (95% CI)</th> <th>RRR (%) (95% CI)</th> </tr> </thead> <tbody> <tr> <td>H₂RA</td> <td>54</td> <td>14</td> <td>7 (5-21)</td> <td>23 (8-35)</td> </tr> <tr> <td>Placebo</td> <td>40</td> <td></td> <td></td> <td></td> </tr> </tbody> </table> <p><small>Moayyedi et al. Cochrane Collaboration 2007</small> <small>Mild asymmetry by funnel plot Small trials with greater effect than larger trials</small></p>		% No or Minimal Symptoms	Therapeutic Gain (%)	NNT (95% CI)	RRR (%) (95% CI)	H ₂ RA	54	14	7 (5-21)	23 (8-35)	Placebo	40								
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<p>T87</p>	<p>Types of Prokinetics</p>	<p>Types of Prokinetics</p> <table border="1"> <thead> <tr> <th></th> <th>Dopamine-2 antagonist</th> <th>5-HT₄ agonist</th> <th>5-HT₃ antagonist</th> <th>Motilin receptor agonist</th> <th>Cholinesterase Inhibitor</th> <th>QT prolongation</th> </tr> </thead> <tbody> <tr> <td>Metoclopramide</td> <td>+</td> <td>+</td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>Domperidone</td> <td>++</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>Cisapride</td> <td></td> <td></td> <td>++</td> <td>+</td> <td></td> <td>++</td> </tr> <tr> <td>Erythromycin, ABT-229</td> <td></td> <td></td> <td></td> <td></td> <td>++</td> <td>++</td> </tr> <tr> <td>Itopride</td> <td>++</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>Tegaserod</td> <td></td> <td></td> <td></td> <td>++</td> <td></td> <td></td> </tr> </tbody> </table> <p><small>Moayyedi P et al. Cochrane Database 2006 T87</small></p>		Dopamine-2 antagonist	5-HT ₄ agonist	5-HT ₃ antagonist	Motilin receptor agonist	Cholinesterase Inhibitor	QT prolongation	Metoclopramide	+	+					Domperidone	++						Cisapride			++	+		++	Erythromycin, ABT-229					++	++	Itopride	++						Tegaserod				++		
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<p>T88</p>	<p>Meta-Analysis of Prokinetic Therapy for Functional Dyspepsia</p>	<p>Meta-Analysis of Prokinetic Therapy for Functional Dyspepsia</p> <ul style="list-style-type: none"> • 19 RCTs (3178 patients) <table border="1"> <thead> <tr> <th></th> <th>% No or Minimal Symptoms</th> <th>Therapeutic Gain (%)</th> <th>NNT (95% CI)</th> <th>RRR (%) (95% CI)</th> </tr> </thead> <tbody> <tr> <td>Prokinetic</td> <td>57</td> <td>10</td> <td>6 (5-12)</td> <td>33 (18-45)</td> </tr> <tr> <td>Placebo</td> <td>47</td> <td></td> <td></td> <td></td> </tr> </tbody> </table> <p>Significant asymmetry by funnel plot</p> <p><small>Moayyedi P et al. Cochrane Database 2006 T88</small></p>		% No or Minimal Symptoms	Therapeutic Gain (%)	NNT (95% CI)	RRR (%) (95% CI)	Prokinetic	57	10	6 (5-12)	33 (18-45)	Placebo	47																																					
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<p>T89</p>	<p>Funnel Plot Prokinetic Trials: Publication Bias?</p>	<p>Funnel Plot Prokinetic Trials: Publication Bias?</p> <p><small>Moayyedi P et al. Cochrane Database 2006 T89</small></p>																																																	

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<p>T90</p>	<p>Metoclopramide for Functional Dyspepsia</p>	<p>Metoclopramide for Functional Dyspepsia</p> <ul style="list-style-type: none"> • Dopaminergic and serotonergic antagonist • Poor quality, older data suggest effects on gastric emptying¹ • No placebo-controlled trials in FD <ul style="list-style-type: none"> • Less effective than cisapride² • Can prolong QT interval and increase prolactin • CNS side effects in up to 20% <ul style="list-style-type: none"> • Anxiety, drowsiness, depression • Extrapyramidal side effects • Tardive dyskinesia <p> ¹Perkel MS et al. Dig Dis Sci 1979; 24:662 ²Fumagalli I and Hammer B. Scand J Gastroenterol 1994; 29:33</p> <p>T90</p>												
<p>T91</p>	<p>Domperidone for Functional Dyspepsia</p>	<p>Domperidone for Functional Dyspepsia</p> <ul style="list-style-type: none"> • 9 double-blind studies (30-60 mg/day) • Peripheral dopaminergic antagonist • Improvement in global assessment without clear effects on gastric emptying • Increases serum prolactin levels <ul style="list-style-type: none"> • Breast tenderness and galactorrhea in <5% • Can prolong QT interval • Not currently available in the US <p> Veldhuyzen Van Zanten SJ et al. Am J Gastroenterol 2001;96: 689 Reddymasu SC et al. Am J Gastroenterol 2007;102:1</p> <p>T91</p>												
<p>T92</p>	<p>Forest Plot of Domperidone Trials for Functional Dyspepsia</p>	<p>Forest Plot of Domperidone Trials for Functional Dyspepsia</p> <p>Relative Risk Meta-Analysis Plot (Random Effects)</p>  <table border="1"> <thead> <tr> <th>Study</th> <th>Relative Risk (95% CI)</th> </tr> </thead> <tbody> <tr> <td>Van Ganse 78</td> <td>0.23 (0.09, 0.52)</td> </tr> <tr> <td>Van de Mierop 79</td> <td>0.34 (0.15, 0.66)</td> </tr> <tr> <td>Davis 88</td> <td>0.39 (0.10, 1.38)</td> </tr> <tr> <td>Chey 82</td> <td>0.10 (0.02, 0.50)</td> </tr> <tr> <td>Combined [random]</td> <td>0.28 (0.17, 0.47)</td> </tr> </tbody> </table> <p>RRR = 72% (95% CI = 83% to 53%) NNT = 2 (95% CI = 1.5 to 3)</p> <p> T92</p>	Study	Relative Risk (95% CI)	Van Ganse 78	0.23 (0.09, 0.52)	Van de Mierop 79	0.34 (0.15, 0.66)	Davis 88	0.39 (0.10, 1.38)	Chey 82	0.10 (0.02, 0.50)	Combined [random]	0.28 (0.17, 0.47)
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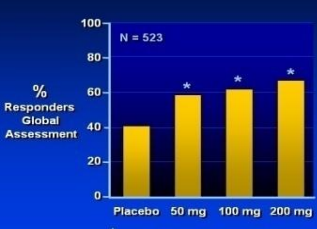
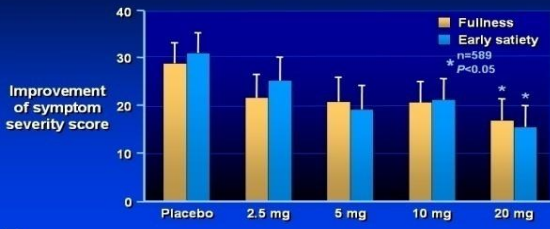
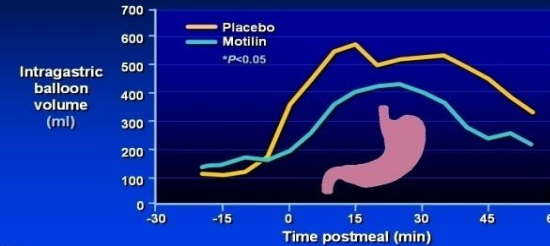
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<p>T93</p>	<p>Cisapride for Functional Dyspepsia: A Meta-Analysis</p>	<p>Cisapride for Functional Dyspepsia: A Meta-Analysis</p> <p>Cisapride : 17 studies</p> <ul style="list-style-type: none"> • 5-HT₄ agonist and 5-HT₃ antagonist • Improvement in global assessment, epigastric pain, early satiety, abdominal distention, nausea • Unclear if accelerated gastric emptying accounts for clinical improvement • No longer available in the US • QT prolongation and cardiac arrhythmias <p><small>Veldhuyzen van Zanten SJ et al. Am J Gastroenterol 2001;96:689 Wysowski DK et al. Am J Gastroenterol 2001;96:1698</small></p> <p><small>T93</small></p>
<p>T94</p>	<p>Tegaserod Accelerates Gastric Emptying</p>	<p>Tegaserod Accelerates Gastric Emptying</p> <p><small>n=12 healthy volunteers P<0.05 Degen L et al. Aliment Pharmacol Ther 2001; 15:1745</small></p> <p><small>T94</small></p>
<p>T95</p>	<p>Effect of Tegaserod on Gastric Accommodation in Functional Dyspepsia</p>	<p>Effect of Tegaserod on Gastric Accommodation in Functional Dyspepsia</p> <p><small>* P < 0,05 n=20 FD patients with normal GE Tack et al., Gastroenterol 2005; 128:A-94 (abs)</small></p> <p><small>T95</small></p>




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<p>T96</p>	<p>Tegaserod for Functional Dyspepsia: Effect on Satisfactory Relief</p>	<p>Tegaserod for Functional Dyspepsia: Effect on Satisfactory Relief</p> <table border="1"> <thead> <tr> <th>Severity</th> <th>Placebo (n)</th> <th>Tegaserod (n)</th> <th>P-value</th> </tr> </thead> <tbody> <tr> <td><Moderate</td> <td>1140</td> <td>1140</td> <td>0.019</td> </tr> <tr> <td>Moderate</td> <td>994</td> <td>994</td> <td>0.0097</td> </tr> <tr> <td>>Moderately severe</td> <td>530</td> <td>530</td> <td>0.0097</td> </tr> </tbody> </table> <p>Vakil N et al. Am J Gastroenterol, submitted</p>	Severity	Placebo (n)	Tegaserod (n)	P-value	<Moderate	1140	1140	0.019	Moderate	994	994	0.0097	>Moderately severe	530	530	0.0097									
Severity	Placebo (n)	Tegaserod (n)	P-value																								
<Moderate	1140	1140	0.019																								
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<p>T97</p>	<p>Alosetron for Functional Dyspepsia: Effect on Adequate Relief</p>	<p>Alosetron for Functional Dyspepsia: Effect on Adequate Relief</p> <table border="1"> <thead> <tr> <th>Dose</th> <th>Total (n)</th> <th>Females (n)</th> <th>Males (n)</th> <th>P-value</th> </tr> </thead> <tbody> <tr> <td>Placebo</td> <td>66</td> <td>66</td> <td>66</td> <td>-</td> </tr> <tr> <td>0.5 mg</td> <td>59</td> <td>59</td> <td>59</td> <td>0.05</td> </tr> <tr> <td>1.0 mg</td> <td>67</td> <td>67</td> <td>67</td> <td>0.05</td> </tr> <tr> <td>2.0 mg</td> <td>65</td> <td>65</td> <td>65</td> <td>0.05</td> </tr> </tbody> </table> <p>Talley NJ et al. Aliment Pharmacol Ther 2001; 15:525</p>	Dose	Total (n)	Females (n)	Males (n)	P-value	Placebo	66	66	66	-	0.5 mg	59	59	59	0.05	1.0 mg	67	67	67	0.05	2.0 mg	65	65	65	0.05
Dose	Total (n)	Females (n)	Males (n)	P-value																							
Placebo	66	66	66	-																							
0.5 mg	59	59	59	0.05																							
1.0 mg	67	67	67	0.05																							
2.0 mg	65	65	65	0.05																							
<p>T98</p>	<p>Levosulpiride or Cisapride for Dysmotility-like Functional Dyspepsia</p>	<p>Levosulpiride or Cisapride for Dysmotility-like Functional Dyspepsia</p> <table border="1"> <thead> <tr> <th>Treatment (n)</th> <th>Baseline (%)</th> <th>8 weeks (%)</th> <th>P-value</th> </tr> </thead> <tbody> <tr> <td>Levosulpiride (69)</td> <td>~18</td> <td>~4</td> <td>0.01</td> </tr> <tr> <td>Cisapride (71)</td> <td>~20</td> <td>~4</td> <td>0.03</td> </tr> </tbody> </table> <p>Levosulpiride is a D₂ antagonist</p> <p>Mearin F et al. Clin Gastroenterol Hepatol 2004;2:301</p>	Treatment (n)	Baseline (%)	8 weeks (%)	P-value	Levosulpiride (69)	~18	~4	0.01	Cisapride (71)	~20	~4	0.03													
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Cisapride (71)	~20	~4	0.03																								

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<p>T99</p>	<p>Itopride for Functional Dyspepsia</p>	<p>Itopride for Functional Dyspepsia</p>  <ul style="list-style-type: none"> • Benzamide with no apparent cardiac toxicity • Prokinetic: Antidopaminergic (D₂) and anti-acetylcholinesterase activity • Maximum benefit was between 100-200 mg tid • No difference in AEs between groups • Phase III trials failed to meet primary outcome <p><i>Holtmann G et al. New Eng J Med 2006; 354:832</i></p>
<p>T100</p>	<p>Motilin Agonist ABT-229: The Disconnect Between Gastric Emptying and Symptoms</p>	<p>Motilin Agonist ABT-229: The Disconnect Between Gastric Emptying and Symptoms</p>  <p><i>Talley NJ et al. Aliment Pharmacol Ther 2000; 14:1653</i></p>
<p>T101</p>	<p>Influence of Motilin on Gastric Accommodation: Stiffens the Fundus</p>	<p>Influence of Motilin on Gastric Accommodation: Stiffens the Fundus</p>  <p><i>Cuomo R et al. Am J Gastroenterol. 2006; 10:804</i></p>

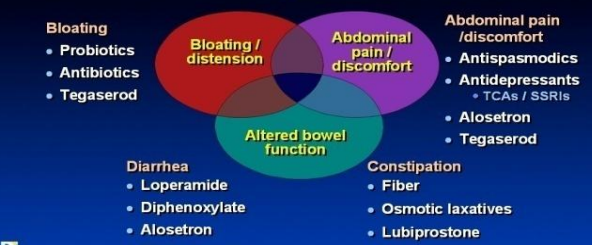

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<p>T102</p>	<p>Investigational Therapies for Functional Dyspepsia</p>	<p>Investigational Therapies for Functional Dyspepsia</p> <ul style="list-style-type: none"> • Antidepressants (SNRIs) • 5-HT₃ antagonists • Selective opioid agonists and antagonists • Somatostatin analogs • Capsaicin • CCK antagonists • CRF antagonists • Neurokinin antagonists • Ghrelin antagonists <p> T102</p>
<p>T103</p>	<p>Herbal Remedies for Functional Dyspepsia: A Systematic Review</p>	<p>Herbal Remedies for Functional Dyspepsia: A Systematic Review</p> <ul style="list-style-type: none"> • 17 RCTs included • 8 had a Jadad score >3 • Peppermint and caraway oils most studied <ul style="list-style-type: none"> • 4 RCTs show benefit • Most studies done with combinations of herbs <ul style="list-style-type: none"> • Effective ingredients unclear • Questionable quality control • Comprehensive safety data unavailable <p> <small>Thompson CJ, Ernst E. <i>Alliment Pharmacol Ther.</i> 2002; 16:1689</small> T103</p>
<p>T104</p>	<p>Other Complimentary Therapies for Functional Dyspepsia</p>	<p>Other Complimentary Therapies for Functional Dyspepsia</p> <ul style="list-style-type: none"> • Recent studies suggest that herbal drug preparation STW 5 affects gastric motility and improves upper GI symptoms^{1,2} • Artichoke leaf extract more effectively improved symptoms and QOL than placebo in patients with functional dyspepsia³ • Capsaicin has been shown in small trials to improve epigastric pain and fullness⁴ <p> <small>¹Pilichiewicz AN et al. <i>AJG</i> 2007; 102:1276 ²Melzer J et al. <i>APT</i> 2004; 20:1279 ³Holtmann G et al. <i>APT</i> 2003; 18:1099 ⁴Bortolotti M et al. <i>APT</i> 2002; 16:1075</small> T104</p>

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<p>T105</p>	<p>STW 5 for Moderate to Severe FD: Results from a Placebo-Controlled, Double-Blind Study</p>	<p>STW 5 for Moderate to Severe FD: Results from a Placebo-Controlled, Double-Blind Study</p> <table border="1"> <caption>GIS Sum Score (M±SD) [Score points]</caption> <thead> <tr> <th>Day</th> <th>STW 5 (n=158)</th> <th>Placebo (n=157)</th> </tr> </thead> <tbody> <tr> <td>Day -7</td> <td>~11.5</td> <td>~11.5</td> </tr> <tr> <td>Day 0</td> <td>~10.5</td> <td>~10.5</td> </tr> <tr> <td>Day 14</td> <td>~6.5</td> <td>~8.0</td> </tr> <tr> <td>Day 28</td> <td>~5.0*</td> <td>~6.5</td> </tr> <tr> <td>Day 56</td> <td>~4.0*</td> <td>~5.0</td> </tr> </tbody> </table> <p>* = P<0,05</p> <p>Von Arnim U et al. Am J Gastroenterol 2007; 102:1268</p>	Day	STW 5 (n=158)	Placebo (n=157)	Day -7	~11.5	~11.5	Day 0	~10.5	~10.5	Day 14	~6.5	~8.0	Day 28	~5.0*	~6.5	Day 56	~4.0*	~5.0
Day	STW 5 (n=158)	Placebo (n=157)																		
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Day 56	~4.0*	~5.0																		
<p>T106</p>	<p>Treatment of Functional Dyspepsia-Epigastric Pain</p>	<p>Treatment of Functional Dyspepsia</p> <p>Epigastric pain</p> <ul style="list-style-type: none"> • Antidepressant or behavioral therapy + <ul style="list-style-type: none"> • Test and treat <i>H pylori</i> and/or • Empiric PPI + <ul style="list-style-type: none"> • Positive diagnosis • Diet, lifestyle advice • Reassurance, OTC treatments • Physician-patient relationship <p>Complementary Therapies?</p> <p>T106</p>																		
<p>T107</p>	<p>Treatment of Functional Dyspepsia-Postprandial Distress</p>	<p>Treatment of Functional Dyspepsia</p> <p>Epigastric pain Postprandial distress</p> <ul style="list-style-type: none"> • Test and treat <i>H pylori</i> and/or • Empiric PPI + <ul style="list-style-type: none"> • Positive diagnosis • Diet, lifestyle advice • Reassurance, OTC treatments • Physician-patient relationship + <ul style="list-style-type: none"> • Antidepressant or behavioral therapies? • Prokinetics • Antiemetics + <ul style="list-style-type: none"> • Positive diagnosis • Diet, lifestyle advice • Reassurance, OTC treatments • Physician-patient relationship <p>Complementary Therapies?</p> <p>T107</p>																		
<p>T108</p>	<p>Section Title-IBS</p>	<p></p>																		

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<p>T109</p>	<p>Pharmacologic Treatments</p>	<p>Pharmacologic Treatments</p>  <ul style="list-style-type: none"> Bloating <ul style="list-style-type: none"> • Probiotics • Antibiotics • Tegaserod Abdominal pain /discomfort <ul style="list-style-type: none"> • Antispasmodics • Antidepressants <ul style="list-style-type: none"> • TCAs / SSRIs • Alosetron • Tegaserod Altered bowel function <ul style="list-style-type: none"> Diarrhea <ul style="list-style-type: none"> • Loperamide • Diphenoxylate • Alosetron • Cholestyramine Constipation <ul style="list-style-type: none"> • Fiber • Osmotic laxatives • Lubiprostone • Tegaserod <p><small>Brandt LJ et al. Am J Gastroenterology 2002; 97(11 Suppl.):S7 Drossman DA et al. Gastroenterology 2002; 123:2108 Saad R, Chey WD. Expert Opin Invest Drugs 2008;17:117</small></p> <p><small>* Tegaserod withdrawn from US in 4/08</small></p> <p>T109</p>																																				
<p>T110</p>	<p>Pharmacotherapy in IBS Should Be Directed to the Dominant Symptom(s)</p>	<p>Pharmacotherapy in IBS: Should Be Directed to the Dominant Symptom(s)</p> <table border="1"> <thead> <tr> <th>Symptom</th> <th>Drug</th> <th>Dose</th> </tr> </thead> <tbody> <tr> <td rowspan="3">Diarrhea</td> <td>Loperamide</td> <td>2-16 mg when necessary</td> </tr> <tr> <td>Cholestyramine</td> <td>4 g with meals</td> </tr> <tr> <td>Alosetron</td> <td>0.5-1.0 mg bid (for severe IBS, females)</td> </tr> <tr> <td rowspan="8">Constipation</td> <td>Psyllium</td> <td>3-4 g bid with meals, and then adjust</td> </tr> <tr> <td>Methylcellulose</td> <td>2 g bid with meals, and then adjust</td> </tr> <tr> <td>Calcium polycarbophil</td> <td>1g qd to qid</td> </tr> <tr> <td>Lactulose</td> <td>10-20 g bid</td> </tr> <tr> <td>Sorbitol</td> <td>15 ml bid</td> </tr> <tr> <td>Polyethylene glycol</td> <td>17 g in 236 liters water qd</td> </tr> <tr> <td>Magnesium hydroxide</td> <td>20-40 ml qd</td> </tr> <tr> <td>Tegaserod</td> <td>6 mg bid</td> </tr> <tr> <td>Lubiprostone</td> <td>8 mcg bid</td> </tr> <tr> <td rowspan="3">Abdominal Pain</td> <td>Smooth muscle relaxant</td> <td>qd to qid ac</td> </tr> <tr> <td>Tricyclic antidepressants</td> <td>Start 25-50 mg hs, and then adjust</td> </tr> <tr> <td>SSRIs</td> <td></td> </tr> </tbody> </table> <p><small>Atkinson W et al. Gut 2004;53:1459 Park M-I and Camilleri M. Neurogastroenterol Motil. 2006;18:595 Uz E et al. J Clin Gastroenterol. 2007;41:380</small></p> <p>T110</p>	Symptom	Drug	Dose	Diarrhea	Loperamide	2-16 mg when necessary	Cholestyramine	4 g with meals	Alosetron	0.5-1.0 mg bid (for severe IBS, females)	Constipation	Psyllium	3-4 g bid with meals, and then adjust	Methylcellulose	2 g bid with meals, and then adjust	Calcium polycarbophil	1g qd to qid	Lactulose	10-20 g bid	Sorbitol	15 ml bid	Polyethylene glycol	17 g in 236 liters water qd	Magnesium hydroxide	20-40 ml qd	Tegaserod	6 mg bid	Lubiprostone	8 mcg bid	Abdominal Pain	Smooth muscle relaxant	qd to qid ac	Tricyclic antidepressants	Start 25-50 mg hs, and then adjust	SSRIs	
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<p>T111</p>	<p>Role of Food Allergy and Intolerance in IBS</p>	<p>Role of Food Allergy and Intolerance in IBS</p> <ul style="list-style-type: none"> • Little data in IBS • Food allergy: rare, usually with atopy (IgE-mediated food hypersensitivity) • Food intolerance: mediated via IgG • Food antigens can activate mucosal immune system and may contribute to food hypersensitivity in IBS • 15% to 71% response rates to elimination diets <ul style="list-style-type: none"> • Yeast, milk, fructose, wheat • Response is dependent upon high adherence  <p><small>Atkinson W et al. Gut 2004;53:1459 Park M-I and Camilleri M. Neurogastroenterol Motil. 2006;18:595 Uz E et al. J Clin Gastroenterol. 2007;41:380</small></p> <p>T111</p>																																				




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<p>T112</p>	<p>Food Elimination Reduces IBS Symptoms</p>	<p>Food Elimination Reduces IBS Symptoms</p> <p>12-week randomized controlled trial with elimination diet based on IgG antibodies to food</p> <table border="1"> <caption>Approximate data from the graph in slide T112</caption> <thead> <tr> <th>Level of Adherence</th> <th>Sham Diet (n=66)</th> <th>True Diet (n=65)</th> </tr> </thead> <tbody> <tr> <td>Low</td> <td>-20</td> <td>-30</td> </tr> <tr> <td>Medium</td> <td>-60</td> <td>-80</td> </tr> <tr> <td>High</td> <td>-65</td> <td>-160</td> </tr> </tbody> </table> <p>Atkinson W et al. Gut 2004; 53:1459</p> <p>T112</p>	Level of Adherence	Sham Diet (n=66)	True Diet (n=65)	Low	-20	-30	Medium	-60	-80	High	-65	-160
Level of Adherence	Sham Diet (n=66)	True Diet (n=65)												
Low	-20	-30												
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<p>T113</p>	<p>Practical Approach to Traditional Therapies</p>	<p>Practical Approach to Traditional Therapies</p> <ul style="list-style-type: none"> • Fiber supplementation <ul style="list-style-type: none"> • Mild constipation symptoms • Start low and titrate up • Gas and bloating • Smooth-muscle relaxants <ul style="list-style-type: none"> • For postprandial abdominal pain • Not effective for chronic abdominal pain • Loperamide <ul style="list-style-type: none"> • Improves diarrhea but not pain • Use preventively <p>T113</p>												
<p>T114</p>	<p>Efficacy of Fiber in IBS-C</p>	<p>Efficacy of Fiber in IBS-C</p> <ul style="list-style-type: none"> • 13 randomized clinical trials <ul style="list-style-type: none"> • Wheat bran, corn fiber, calcium polycarbophil, ispaghula, and psyllium • Low-intermediate quality studies with small sample sizes • Ispaghula (4/5 studies) improved global IBS symptoms and ease of stool passage but not pain. • Side effects: may increase intestinal gas, bloating and abdominal discomfort • Appropriate for constipation-predominant symptoms <p>Brandt LJ et al. Am J Gastroenterol 2002;97 suppl:S7-26 Lesbros-Pantoflickova D et al. Aliment Pharmacol Ther 2004;20:1253</p> <p>T114</p>												

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<p>T115</p>	<p>Fiber/Bulking Agents for IBS: Effect on Global Symptoms</p>	<table border="1"> <caption>Fiber/Bulking Agents for IBS: Effect on Global Symptoms</caption> <thead> <tr> <th>Study</th> <th>Quality score</th> <th>(n/N)</th> <th>(n/N)</th> <th>95% CI random</th> </tr> </thead> <tbody> <tr><td>Arthurs</td><td>3</td><td>29/40</td><td>24/38</td><td></td></tr> <tr><td>Cook</td><td>4</td><td>3/14</td><td>4/14</td><td></td></tr> <tr><td>Fowlie</td><td>3</td><td>15/25</td><td>17/24</td><td></td></tr> <tr><td>Jalilhal</td><td>2</td><td>7/20</td><td>2/20</td><td></td></tr> <tr><td>Longstreth</td><td>4</td><td>20/26</td><td>24/34</td><td></td></tr> <tr><td>Lucey</td><td>2</td><td>22/28</td><td>20/28</td><td></td></tr> <tr><td>Nigam</td><td>2</td><td>41/84</td><td>22/84</td><td></td></tr> <tr><td>Prior</td><td>4</td><td>66/80</td><td>42/80</td><td></td></tr> <tr><td>Ritchie, 1979</td><td>2</td><td>33/48</td><td>23/48</td><td></td></tr> <tr><td>Ritchie, 1980</td><td>2</td><td>20/28</td><td>8/28</td><td></td></tr> <tr><td>Snook</td><td>4</td><td>37/71</td><td>38/71</td><td></td></tr> <tr><td>Soltsoft</td><td>3</td><td>15/29</td><td>15/23</td><td></td></tr> <tr><td>Toskes</td><td>2</td><td>23/48</td><td>13/48</td><td></td></tr> <tr><td>Total (95% CI)</td><td></td><td>344/557</td><td>263/556</td><td></td></tr> <tr><td>Total high-quality studies (95% CI)</td><td></td><td>344/285</td><td>164/284</td><td></td></tr> </tbody> </table> <p>Lesbros-Pantoflickova D et al. APT 2004; 20:1253 T115</p>	Study	Quality score	(n/N)	(n/N)	95% CI random	Arthurs	3	29/40	24/38		Cook	4	3/14	4/14		Fowlie	3	15/25	17/24		Jalilhal	2	7/20	2/20		Longstreth	4	20/26	24/34		Lucey	2	22/28	20/28		Nigam	2	41/84	22/84		Prior	4	66/80	42/80		Ritchie, 1979	2	33/48	23/48		Ritchie, 1980	2	20/28	8/28		Snook	4	37/71	38/71		Soltsoft	3	15/29	15/23		Toskes	2	23/48	13/48		Total (95% CI)		344/557	263/556		Total high-quality studies (95% CI)		344/285	164/284	
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<p>T116</p>	<p>Antispasmodics in IBS</p>	<p>Antispasmodics in IBS</p> <ul style="list-style-type: none"> • Cause smooth-muscle relaxation by either <ul style="list-style-type: none"> ◦ Direct effect (eg, mebeverine, pinaverium) ◦ Anticholinergic or antimuscarinic properties (eg, dicyclomine, hyoscamine) • Meta-analysis of 24 RCTs <ul style="list-style-type: none"> ◦ Only octylonium bromide was effective in relieving global IBS symptoms ◦ Mainly inconclusive findings due to heterogeneity of trials, and small sample sizes • Side effects: dry mouth, constipation, urinary retention and visual disturbances <p>Lesbros-Pantoflickova D et al. Aliment Pharmacol Ther. 2004; 20:1253 T116</p>																																																																																
<p>T117</p>	<p>Efficacy of Antispasmodics in IBS</p>	<table border="1"> <caption>Efficacy of Antispasmodics in IBS</caption> <thead> <tr> <th>Study</th> <th>Treatment n/N</th> <th>Control n/N</th> <th>OR 95% CI random</th> </tr> </thead> <tbody> <tr><td>Pinaverium bromide</td><td></td><td></td><td></td></tr> <tr><td>Subtotal (95% CI)</td><td>43/55</td><td>34/55</td><td>2.2 (1.0 - 4.5)</td></tr> <tr><td>Subtotal high quality (95%)</td><td>19/25</td><td>17/25</td><td>1.5 (0.4 - 5.0)</td></tr> <tr><td>Cimetropium bromide</td><td></td><td></td><td></td></tr> <tr><td>Subtotal (95% CI)</td><td>58/87</td><td>34/86</td><td>3.1 (1.7 - 6.7)</td></tr> <tr><td>Subtotal high quality (95%)</td><td>30/48</td><td>28/47</td><td>1.1 (0.5 - 2.6)</td></tr> <tr><td>Octylonium bromide</td><td></td><td></td><td></td></tr> <tr><td>Subtotal (95% CI)</td><td>180/383</td><td>115/391</td><td>2.2 (1.6 - 2.9)</td></tr> <tr><td>Subtotal high quality (95%)</td><td>148/317</td><td>102/325</td><td>1.9 (1.4 - 2.7)</td></tr> <tr><td>Mebeverine</td><td></td><td></td><td></td></tr> <tr><td>Subtotal (95% CI)</td><td>63/122</td><td>44/119</td><td>2.0 (1.2 - 3.6)</td></tr> <tr><td>Subtotal high quality (95%)</td><td>6/40</td><td>12/40</td><td>0.4 (0.1 - 1.2)</td></tr> <tr><td>Hyoscine</td><td></td><td></td><td></td></tr> <tr><td>Subtotal (95% CI)</td><td>166/314</td><td>130/310</td><td>1.6 (1.1 - 2.2)</td></tr> <tr><td>Subtotal high quality (95%)</td><td>106/182</td><td>91/178</td><td>1.3 (0.9 - 2.0)</td></tr> <tr><td>Total (95% CI)</td><td>614/1138</td><td>130/1125</td><td>2.1 (1.8 - 2.9)</td></tr> <tr><td>Total high quality (95%)</td><td>309/612</td><td>250/615</td><td>1.5 (1.2 - 1.9)</td></tr> </tbody> </table> <p>Lesbros-Pantoflickova D et al. Aliment Pharmacol Ther 2004; 20:1253 T117</p>	Study	Treatment n/N	Control n/N	OR 95% CI random	Pinaverium bromide				Subtotal (95% CI)	43/55	34/55	2.2 (1.0 - 4.5)	Subtotal high quality (95%)	19/25	17/25	1.5 (0.4 - 5.0)	Cimetropium bromide				Subtotal (95% CI)	58/87	34/86	3.1 (1.7 - 6.7)	Subtotal high quality (95%)	30/48	28/47	1.1 (0.5 - 2.6)	Octylonium bromide				Subtotal (95% CI)	180/383	115/391	2.2 (1.6 - 2.9)	Subtotal high quality (95%)	148/317	102/325	1.9 (1.4 - 2.7)	Mebeverine				Subtotal (95% CI)	63/122	44/119	2.0 (1.2 - 3.6)	Subtotal high quality (95%)	6/40	12/40	0.4 (0.1 - 1.2)	Hyoscine				Subtotal (95% CI)	166/314	130/310	1.6 (1.1 - 2.2)	Subtotal high quality (95%)	106/182	91/178	1.3 (0.9 - 2.0)	Total (95% CI)	614/1138	130/1125	2.1 (1.8 - 2.9)	Total high quality (95%)	309/612	250/615	1.5 (1.2 - 1.9)								
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Computer-Based Learning Program
Treatment

<p>T118</p>	<p>Loperamide for IBS-D</p>	<p>Loperamide for IBS-D</p> <ul style="list-style-type: none"> • Only antidiarrheal studied in IBS • Three RCTs of low-intermediate quality • Decreased stool frequency and improved stool consistency but not abdominal pain or global IBS symptoms • Most appropriate for patients with diarrhea-predominant symptoms <p> Brandt LJ et al. Am J Gastroenterol 2002; 97 suppl:S7</p> <p>T118</p>																								
<p>T119</p>	<p>The Role of Neurotransmitters in GI Function</p>	<p>The Role of Neurotransmitters in GI Function</p> <table border="1"> <thead> <tr> <th>Motility</th> <th>Visceral sensation</th> <th>Secretion</th> </tr> </thead> <tbody> <tr> <td>Serotonin (5-HT)</td> <td>Serotonin (5-HT)</td> <td>Serotonin (5-HT)</td> </tr> <tr> <td>Acetylcholine</td> <td>Tachykinin</td> <td>Acetylcholine</td> </tr> <tr> <td>Nitric oxide</td> <td>Calcitonin gene-related peptide</td> <td>Vasoactive intestinal peptide</td> </tr> <tr> <td>Substance P</td> <td>Neurokinin A</td> <td></td> </tr> <tr> <td>Vasoactive intestinal Peptide</td> <td>Enkephalins</td> <td></td> </tr> <tr> <td>Cholecystokinin</td> <td>CRF</td> <td></td> </tr> <tr> <td>Corticotropin releasing factor (CRF)</td> <td></td> <td></td> </tr> </tbody> </table> <p> Crowell MD, Wessinger SB. Expert Opin Investig Drugs 2007;16:761 Lacy BE, Yu S. J Clin Gastroenterol 2002;34:27</p> <p>T119</p>	Motility	Visceral sensation	Secretion	Serotonin (5-HT)	Serotonin (5-HT)	Serotonin (5-HT)	Acetylcholine	Tachykinin	Acetylcholine	Nitric oxide	Calcitonin gene-related peptide	Vasoactive intestinal peptide	Substance P	Neurokinin A		Vasoactive intestinal Peptide	Enkephalins		Cholecystokinin	CRF		Corticotropin releasing factor (CRF)		
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Treatment

<p>T121</p>	<p>Efficacy of Alosetron in IBS: A Meta-Analysis of RCTs</p>	<p>Efficacy of Alosetron in IBS: A Meta-Analysis of RCTs</p> <table border="1"> <thead> <tr> <th>Study</th> <th>Odds ratios (95% CI)</th> </tr> </thead> <tbody> <tr> <td>Camilleri et al.</td> <td>1.28 (0.98, 1.67)</td> </tr> <tr> <td>Jones et al.</td> <td>1.69 (1.42, 2.32)</td> </tr> <tr> <td>Bardhan et al.</td> <td>1.6 (0.93, 2.63)</td> </tr> <tr> <td>Camilleri et al.</td> <td>1.35 (0.98, 1.83)</td> </tr> <tr> <td>Camilleri et al.</td> <td>1.99 (1.45, 2.71)</td> </tr> <tr> <td>Lembo et al.</td> <td>2.76 (2.04, 3.72)</td> </tr> <tr> <td>Pooled (excluding alosetrone and mebeverine)</td> <td>1.85 (1.57, 2.18)</td> </tr> <tr> <td>Pooled (all studies)</td> <td>1.81 (1.57, 2.10)</td> </tr> </tbody> </table> <p>Cremonini F et al. Neurogastroenterol Motil. 2003; 15:79</p>	Study	Odds ratios (95% CI)	Camilleri et al.	1.28 (0.98, 1.67)	Jones et al.	1.69 (1.42, 2.32)	Bardhan et al.	1.6 (0.93, 2.63)	Camilleri et al.	1.35 (0.98, 1.83)	Camilleri et al.	1.99 (1.45, 2.71)	Lembo et al.	2.76 (2.04, 3.72)	Pooled (excluding alosetrone and mebeverine)	1.85 (1.57, 2.18)	Pooled (all studies)	1.81 (1.57, 2.10)																								
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<p>T122</p>	<p>Alosetron Improves Global Symptoms in Women with Severe IBS-D</p>	<p>Alosetron Improves Global Symptoms in Women with Severe IBS-D</p> <table border="1"> <thead> <tr> <th>Treatment</th> <th>N</th> <th>% GIS Responders</th> </tr> </thead> <tbody> <tr> <td>Placebo</td> <td>176</td> <td>~30</td> </tr> <tr> <td>0.5mg qd</td> <td>177</td> <td>~50*</td> </tr> <tr> <td>1mg qd</td> <td>175</td> <td>~48*</td> </tr> <tr> <td>1mg bid</td> <td>177</td> <td>~43*</td> </tr> </tbody> </table> <p>*P<0.02 vs placebo Assessment at 12 weeks GIS = Global Improvement Scale</p> <p>Krause R et al. Am J Gastroenterol 2007; 102:1709</p>	Treatment	N	% GIS Responders	Placebo	176	~30	0.5mg qd	177	~50*	1mg qd	175	~48*	1mg bid	177	~43*																											
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Treatment

<p>T124</p>	<p>Safety Profile of Alosetron</p>	<p>Safety Profile of Alosetron</p> <ul style="list-style-type: none"> • Black-box warning: serious GI effects • Ischemic colitis <ul style="list-style-type: none"> • 2 per 1000 patients over 3 months • 3 per 1000 patients over 6 months • Constipation <ul style="list-style-type: none"> • Alosetron (1 mg bid), 29% • Placebo, 6% • No clinically relevant drug-drug interactions • Pregnancy category B <p> Alosetron [package insert]. GlaxoSmithKline; 2006</p> <p style="text-align: right;">T124</p>																
<p>T125</p>	<p>Indications for Restricted Use of Alosetron</p>	<p>Indications for Restricted Use of Alosetron</p> <ul style="list-style-type: none"> • Only for women with severe diarrhea-predominant IBS who have <ul style="list-style-type: none"> • Chronic IBS symptoms (\geq 6 months) • No evidence of anatomic or biochemical abnormalities of the GI tract • Failed to respond to conventional therapy • IBS is severe if it includes diarrhea and \geq1 of the following: <ul style="list-style-type: none"> • Frequent, severe abdominal pain / discomfort • Frequent bowel urgency or fecal incontinence • Disability or restriction of daily activities due to IBS <p> Harris LA, Chang L. Women's Health 2007; 3:15</p> <p style="text-align: right;">T125</p>																
<p>T126</p>	<p>Ischemic Colitis in the General Population and IBS Patients Taking Alosetron</p>	<p>Ischemic Colitis in the General Population and IBS Patients Taking Alosetron</p> <table border="1" data-bbox="1396 987 1879 1209"> <thead> <tr> <th>Group</th> <th>Reported cases</th> </tr> </thead> <tbody> <tr> <td>General population^{1,2}</td> <td>7¹ to 47/100,000² patient-years</td> </tr> <tr> <td>IBS^{1,2}</td> <td>43¹ to 179/100,000² patient-years</td> </tr> <tr> <td colspan="2">Alosetron^{1,3}</td> </tr> <tr> <td> Clinical trials</td> <td>590¹ to 674³/100,000 patient-years</td> </tr> <tr> <td> Alosetron</td> <td>110/100,000 patient-years</td> </tr> <tr> <td> Placebo</td> <td>110/100,000³ patient-years</td> </tr> <tr> <td> Post-marketing</td> <td>(210/100,000 after re-introduction)</td> </tr> </tbody> </table> <p> ¹Cole JA et al. Am J Gastro. 2004;99:486 ²Chang L et al. Am J Gastro 2006;101:1069 ³Singh G et al. Gastroenterology. 2004;126:A349</p> <p style="text-align: right;">T126</p>	Group	Reported cases	General population ^{1,2}	7 ¹ to 47/100,000 ² patient-years	IBS ^{1,2}	43 ¹ to 179/100,000 ² patient-years	Alosetron^{1,3}		Clinical trials	590 ¹ to 674 ³ /100,000 patient-years	Alosetron	110/100,000 patient-years	Placebo	110/100,000 ³ patient-years	Post-marketing	(210/100,000 after re-introduction)
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<p>T127</p>	<p>Tegaserod Improves Global Symptoms in IBS-C</p>	<p>Tegaserod Improves Global Symptoms in IBS-C</p> <p>International: Tegaserod 6 mg bid (females n=244, males n=50) vs Placebo (females n=240, males n=48). P<0.05 vs placebo ITT.</p> <p>Asia Pacific: Tegaserod 6 mg bid (females n=226, males n=33) vs Placebo (females n=232, males n=29). P<0.05; ** P<0.01 vs placebo ITT.</p> <p>Tegaserod produced a significantly greater response rate than placebo</p> <p>Müller-Lissner SA et al. <i>Aliment Pharmacol Ther.</i> 2001; 15:1655 Kellow J et al. <i>Gut</i> 2003; 52:674</p> <p>T127</p>												
<p>T128</p>	<p>Safety Profile of Tegaserod</p>	<p>Safety Profile of Tegaserod</p> <ul style="list-style-type: none"> • Common side effects: diarrhea (7-9%), headache (11%), and nasopharyngitis (7%) • Precaution: ischemic colitis <ul style="list-style-type: none"> • No cases in clinical trials and small number in post-marketing surveillance • No clinically relevant drug-drug interactions • Pregnancy category B • Restricted access in US market related to increased cardiovascular events in clinical trials <p>Müller-Lissner S et al. <i>Aliment Pharmacol Ther.</i> 2001; 15:1655 Tougas G et al. <i>Aliment Pharmacol Ther.</i> 2002; 16:1701 www.fda.gov/ibsttopics/NEWS/2007/NEW01673.htm</p> <p>T128</p>												
<p>T129</p>	<p>Tegaserod</p>	<p>Tegaserod</p> <ul style="list-style-type: none"> • Suspended from the US market – March 30, 2007 <ul style="list-style-type: none"> • Increased incidence of CV events and CVAs between those randomized to tegaserod vs. placebo in clinical trials <table border="1"> <thead> <tr> <th></th> <th># Events</th> <th>Total patients</th> <th>Incidence</th> </tr> </thead> <tbody> <tr> <td>Tegaserod</td> <td>13</td> <td>11,614</td> <td>0.11%*</td> </tr> <tr> <td>Placebo</td> <td>1</td> <td>7,031</td> <td>0.01%</td> </tr> </tbody> </table> <ul style="list-style-type: none"> • Restricted use program – July 2007 <ul style="list-style-type: none"> • For women aged < 55 with chronic idiopathic constipation or IBS-C <p>* P=0.02; 3 MIs, one sudden cardiac death, 6 unstable angina, 3 CVAs (blinded, adjudicated data) Tegaserod pts who developed events had a history of cardiac disease or risk factors</p> <p>US FDA Web site. http://www.fda.gov/cder/drug/advisory/tegaserod.htm</p> <p>T129</p>		# Events	Total patients	Incidence	Tegaserod	13	11,614	0.11%*	Placebo	1	7,031	0.01%
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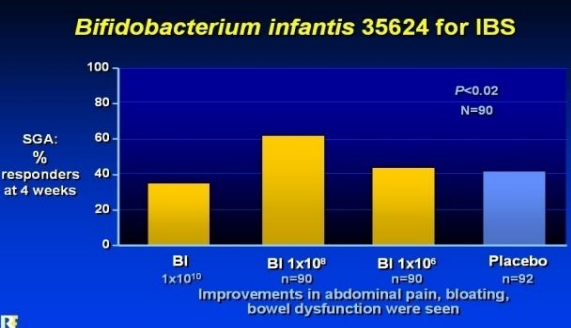
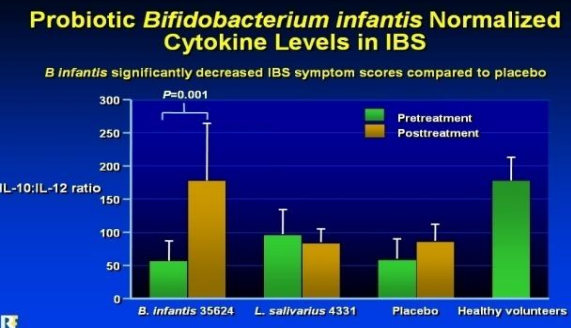

Computer-Based Learning Program
Treatment

<p>T130</p>	<p>Lubiprostone for IBS-C: Data from 2 Phase III Trials</p>	<p>Lubiprostone for IBS-C: Data from 2 Phase III Trials</p> <ul style="list-style-type: none"> 12-week treatment period Overall responder=monthly responder for at least 2 of 3 months Monthly responder=at least moderate relief for 4/4 weeks or significant relief for 2/4 weeks <table border="1"> <thead> <tr> <th>Treatment</th> <th>n</th> <th>% Overall Responders</th> </tr> </thead> <tbody> <tr> <td>Lubiprostone 8 mcg bid</td> <td>780</td> <td>17.9</td> </tr> <tr> <td>Placebo</td> <td>387</td> <td>10.1</td> </tr> </tbody> </table> <p><i>Drossman DA et al. Gastroenterology 2007; 132:639f</i></p>	Treatment	n	% Overall Responders	Lubiprostone 8 mcg bid	780	17.9	Placebo	387	10.1							
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Lubiprostone 8 mcg bid	780	17.9																
Placebo	387	10.1																
<p>T131</p>	<p>Incidence of Nausea with Lubiprostone in Clinical Trials</p>	<p>Incidence of Nausea with Lubiprostone in Clinical Trials</p> <ul style="list-style-type: none"> Chronic idiopathic constipation: 24 mcg bid with food Irritable bowel syndrome with constipation: 8 mcg bid with food <table border="1"> <thead> <tr> <th>Trial Group</th> <th>Subgroup</th> <th>% Incidence</th> </tr> </thead> <tbody> <tr> <td rowspan="3">Phase II & III Trials in Chronic Constipation (24-mcg-bid dose)</td> <td>Total</td> <td>~30</td> </tr> <tr> <td>Elderly > 65</td> <td>~18</td> </tr> <tr> <td>Men</td> <td>~8</td> </tr> <tr> <td rowspan="1">Phase III Trials in IBS-C (8-mcg-bid dose)</td> <td>Total</td> <td>~8</td> </tr> </tbody> </table> <p><i>Saad R, Chey WD. Exp Review Gastroenterol Hepatol. In press.</i></p>	Trial Group	Subgroup	% Incidence	Phase II & III Trials in Chronic Constipation (24-mcg-bid dose)	Total	~30	Elderly > 65	~18	Men	~8	Phase III Trials in IBS-C (8-mcg-bid dose)	Total	~8			
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<p>T132</p>	<p>Effect of Linaclotide on Colonic Transit in IBS-C</p>	<p>Effect of Linaclotide on Colonic Transit in IBS-C</p> <ul style="list-style-type: none"> Mean + SEM Baseline Post treatment <table border="1"> <thead> <tr> <th>Treatment</th> <th>n</th> <th>Baseline GC 48</th> <th>Post-treatment GC 48</th> </tr> </thead> <tbody> <tr> <td>Placebo</td> <td>12</td> <td>~2.8</td> <td>~3.1</td> </tr> <tr> <td>Linaclotide 100 mg</td> <td>12</td> <td>~2.8</td> <td>~3.2</td> </tr> <tr> <td>Linaclotide 1000 mg</td> <td>12</td> <td>~2.8</td> <td>~3.8*</td> </tr> </tbody> </table> <p><i>Andresen V et al. Gastroenterology 2007; 133:761</i></p> <p>*P=0.01 vs placebo GC 48 = geometric center at 48 hours</p>	Treatment	n	Baseline GC 48	Post-treatment GC 48	Placebo	12	~2.8	~3.1	Linaclotide 100 mg	12	~2.8	~3.2	Linaclotide 1000 mg	12	~2.8	~3.8*
Treatment	n	Baseline GC 48	Post-treatment GC 48															
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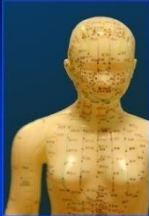
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<p>T133</p>	<p>Effect of Rifaximin in Patients with Bloating <i>Without</i> SIBO</p>	<p>Effect of Rifaximin in Patients With Bloating <i>Without</i> SIBO</p> <p>Overall Study Population</p> <table border="1"> <thead> <tr> <th>Time Point</th> <th>Rifaximin (n=63) (%)</th> <th>Placebo (n=61) (%)</th> </tr> </thead> <tbody> <tr> <td>Baseline</td> <td>0</td> <td>0</td> </tr> <tr> <td>Treatment completion</td> <td>~40*</td> <td>~20</td> </tr> <tr> <td>Post-treatment</td> <td>~25*</td> <td>~10</td> </tr> </tbody> </table> <p>IBS only</p> <table border="1"> <thead> <tr> <th>Time Point</th> <th>Rifaximin (n=63) (%)</th> <th>Placebo (n=61) (%)</th> </tr> </thead> <tbody> <tr> <td>Baseline</td> <td>0</td> <td>0</td> </tr> <tr> <td>Treatment completion</td> <td>~40*</td> <td>~20</td> </tr> <tr> <td>Post-Treatment</td> <td>~25*</td> <td>~10</td> </tr> </tbody> </table> <p>Rifaximin 400mg bid x 10 days; post-tx: 10 days Global endpoint: symptom improvement * P < 0.05</p> <p>Shahara AI et al. Am J Gastroenterol, 2006; 101:326 T133</p>	Time Point	Rifaximin (n=63) (%)	Placebo (n=61) (%)	Baseline	0	0	Treatment completion	~40*	~20	Post-treatment	~25*	~10	Time Point	Rifaximin (n=63) (%)	Placebo (n=61) (%)	Baseline	0	0	Treatment completion	~40*	~20	Post-Treatment	~25*	~10
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<p>T135</p>	<p>Antibiotics for IBS: Points to Consider</p>	<p>Antibiotics for IBS: Points to Consider</p> <ul style="list-style-type: none"> • Reasons for symptom improvement are unclear <ul style="list-style-type: none"> ◦ SIBO vs alteration of colonic flora? • Optimal diagnostic test for SIBO unclear <ul style="list-style-type: none"> ◦ Breath test results may not predict response to antibiotics • Optimal antibiotic therapy unclear • Benefits appear transient • Potential consequences of repeated, widespread antibiotic use? <p>T135</p>																								

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<p>T136</p>	<p><i>Bifidobacterium infantis</i> 35624 for IBS</p>	<p><i>Bifidobacterium infantis</i> 35624 for IBS</p>  <p>SGA: % responders at 4 weeks</p> <p>$P < 0.02$ $N = 90$</p> <p>BI 1×10^9 BI 1×10^8 BI 1×10^6 Placebo</p> <p>Improvements in abdominal pain, bloating, bowel dysfunction were seen</p> <p>Whorwell PJ et al. J Gastroenterol 2006; 101:1581</p> <p>T136</p>
<p>T137</p>	<p>Probiotic <i>Bifidobacterium infantis</i> Normalized Cytokine Levels in IBS</p>	<p>Probiotic <i>Bifidobacterium infantis</i> Normalized Cytokine Levels in IBS</p> <p><i>B. infantis</i> significantly decreased IBS symptom scores compared to placebo</p>  <p>IL-10:IL-12 ratio</p> <p>$P = 0.001$</p> <p>■ Pretreatment ■ Posttreatment</p> <p>B. <i>infantis</i> 35624 L. <i>salivarius</i> 4331 Placebo Healthy volunteers</p> <p>O'Mahoney L et al. Gastroenterology 2005; 128:541</p> <p>T137</p>
<p>T138</p>	<p>Complementary Therapy for IBS: Chinese Herbal Therapy</p>	<p>Complementary Therapy for IBS: Chinese Herbal Therapy</p> <ul style="list-style-type: none"> • Two of three randomized controlled trials¹⁻³ found that Chinese herbal therapy was more effective than placebo <ul style="list-style-type: none"> • Greater benefits with individualized herbal preparation¹ • Studies used different herbal combinations • Specific herbs that offer benefit, mechanism of action, long-term safety, and potential drug interactions are unclear  <p>¹Bensoussan A et al. JAMA 1998; 280:1585 ²Madisch A et al. Aliment Pharmacol Ther. 2004; 19:271 ³Leung WK et al. Am J Gastroenterol. 2006;101:1574</p> <p>T138</p>

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<p>T139</p>	<p>Complementary Therapy for IBS: Acupuncture</p>	<p>Complementary Therapy for IBS: Acupuncture</p>  <ul style="list-style-type: none"> • A recent systematic review evaluated six randomized placebo-controlled treatment trials in IBS¹ <ul style="list-style-type: none"> • Low-quality studies with inconclusive results • No clear benefit on IBS symptoms compared to sham acupuncture • Effects of acupuncture on rectal perception <ul style="list-style-type: none"> • No effect on rectal sensation in IBS in one study² and decreased perception in the other³ <p><small>¹Lim B et al. Cochrane Database 2008. ²Xing J et al. Altern Ther Health Med. 2004; 10:38 ³Schneider A et al. Gut 2006; 55:649</small></p> <p style="text-align: right;">R T139</p>
<p>T140</p>	<p>Drugs in Development for IBS-D</p>	<p>Drugs in Development for IBS-D</p> <ul style="list-style-type: none"> • Crofelemer: Reduces chloride secretion <ul style="list-style-type: none"> • Phase II trial found improvements in abdominal pain and a trend toward improvement in stool frequency¹ • R-verapamil: Calcium channel antagonist <ul style="list-style-type: none"> • Phase II trials suggest benefit for global symptoms² • Further studies are planned in North America <p><small>¹Lembo AJ et al. Gastroenterology 2007; 132:A141 ²Quigley EM et al. Am J Gastroenterol 2007;102(S2):S502</small></p> <p style="text-align: right;">R T140</p>
<p>T141</p>	<p>Autonomic Modulators</p>	<p>Autonomic Modulators</p> <ul style="list-style-type: none"> • α_2 Agonists: Clonidine,¹ AGN 203818 <ul style="list-style-type: none"> • Improved bowel dysfunction (firmer stools and easier stool passage) with clonidine vs placebo • Benzodiazepine derivatives: Dextofisopam² <ul style="list-style-type: none"> • Overall relief of symptoms in IBS-D and IBS-A • Also improved stool consistency and frequency • Corticotropin releasing factor (CRF) antagonist³ <ul style="list-style-type: none"> • Reduced the increase in abdominal pain and anxiety evoked by electrical stimulation in the rectum in IBS <p><small>¹Camilleri M et al. Clin Gastroenterol and Hepatol. 2003; 1:111 ²Leventer et al. Gastroenterology 2005; 128: A-94 ³Sagami S et al. Gut 2004; 53:958</small></p> <p style="text-align: right;">R T141</p>

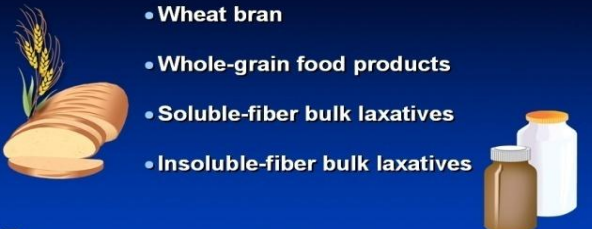
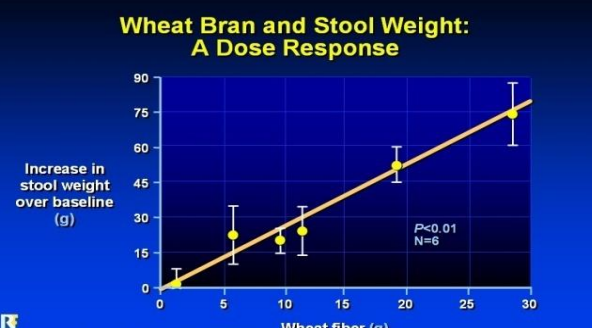
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<p>T142</p>	<p>Renzapride, a 5-HT₄ Agonist / 5-HT₃ Antagonist, Accelerates Colonic Transit in Patients with IBS-C</p>	<p>Renzapride, a 5-HT₄-Agonist / 5-HT₃-Antagonist, Accelerates Colonic Transit in Patients with IBS-C</p> <p>Camilleri M et al. Clin Gastroenterol Hepatol 2004; 2:895</p>																																			
<p>T143</p>	<p>Emerging Therapies for IBS</p>	<p>Emerging Therapies for IBS</p> <p>Saad R, Chey WD. Expert Opin Invest Drugs. 2008;17:117</p>																																			
<p>T144</p>	<p>Evidence-Based Summary of Medical Therapies for IBS-C</p>	<p>Evidence-Based Summary of Medical Therapies for IBS-C</p> <table border="1"> <thead> <tr> <th></th> <th>Global Symptoms</th> <th>Pain</th> <th>Bloating</th> <th>Stool Frequency</th> <th>Stool Consistency</th> <th>Evidence</th> </tr> </thead> <tbody> <tr> <td>Fiber</td> <td></td> <td></td> <td></td> <td>+</td> <td>+</td> <td>B</td> </tr> <tr> <td>Laxatives</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>Insufficient evidence</td> </tr> <tr> <td>Tegaserod</td> <td>+</td> <td>+/-</td> <td>+</td> <td>+</td> <td>+</td> <td>A</td> </tr> <tr> <td>Lubiprostone</td> <td>+</td> <td>+</td> <td></td> <td></td> <td>+</td> <td>A</td> </tr> </tbody> </table> <p>Ⓡ</p>		Global Symptoms	Pain	Bloating	Stool Frequency	Stool Consistency	Evidence	Fiber				+	+	B	Laxatives						Insufficient evidence	Tegaserod	+	+/-	+	+	+	A	Lubiprostone	+	+			+	A
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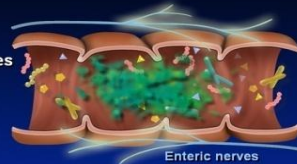
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<p>T145</p>	<p>Evidence-Based Summary of Medical Therapies for IBS-D</p>	<p>Evidence-Based Summary of Medical Therapies for IBS-D</p> <table border="1"> <thead> <tr> <th></th> <th>Global Symptoms</th> <th>Pain</th> <th>Urgency</th> <th>Stool Frequency</th> <th>Stool Consistency</th> <th>Evidence</th> </tr> </thead> <tbody> <tr> <td>Fiber</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>Insufficient evidence</td> </tr> <tr> <td>Loperimide</td> <td></td> <td></td> <td>+</td> <td>+</td> <td>+</td> <td>B</td> </tr> <tr> <td>Anti-Spasmotics</td> <td>+/-</td> <td>+</td> <td></td> <td></td> <td></td> <td>B</td> </tr> <tr> <td>Alosetron</td> <td>+</td> <td>+</td> <td>+</td> <td>+</td> <td>+</td> <td>A</td> </tr> </tbody> </table> <p><small>T145</small></p>		Global Symptoms	Pain	Urgency	Stool Frequency	Stool Consistency	Evidence	Fiber						Insufficient evidence	Loperimide			+	+	+	B	Anti-Spasmotics	+/-	+				B	Alosetron	+	+	+	+	+	A
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<p>T146</p>	<p>Section Title: Constipation</p>																																				
<p>T147</p>	<p>Functional Constipation</p>	<p>Functional Constipation</p> <p>↓ Exclude Red Flags</p> <p>Reassurance, General Measures, Increase Dietary Fiber</p> <p>↓ No Response</p> <p>Bulking Agents: Psyllium, Methylcellulose, Ca polycarbophil</p> <p>↓</p> <table border="1"> <tr> <td>Osmotic Laxatives: Unabsorbed CHOs PEG Saline laxatives</td> <td>Stimulant Laxatives: Bisacodyl, Senna Cascara</td> <td>Chloride Channels Activators: Lubiprostone</td> <td>Prokinetics: Tegaserod</td> </tr> </table> <p>↓ No Response</p> <p>Consider: Switching Agent, Combining Therapies Further Investigations</p> <p><small>T147</small></p>	Osmotic Laxatives: Unabsorbed CHOs PEG Saline laxatives	Stimulant Laxatives: Bisacodyl, Senna Cascara	Chloride Channels Activators: Lubiprostone	Prokinetics: Tegaserod																															
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<p>T148</p>	<p>General Measures for Constipation</p>	<p>General Measures for Constipation</p> <p><small>T148</small></p>																																			








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<p>T149</p>	<p>Medications Associated With Constipation</p>	<p>Medications Associated With Constipation</p> <p>Nonprescription drugs</p> <ul style="list-style-type: none"> Antacids, especially calcium-containing Calcium supplements Iron supplements Antidiarrheal agents Nonsteroidal antiinflammatory agents <p>Prescription drugs</p> <ul style="list-style-type: none"> Opioids Anticholinergic agents Tricyclic antidepressants Calcium channel blockers Statin agents Anti-Parkinsonian drugs Sympathomimetics Antipsychotics Diuretics Antihistamines <p><small>Locke GR III et al. Gastroenterology 2000; 119:1766</small></p>
<p>T150</p>	<p>Fiber Supplementation and Bulk Laxatives Classification</p>	<p>Fiber Supplementation and Bulk Laxatives Classification</p> <ul style="list-style-type: none"> • Wheat bran • Whole-grain food products • Soluble-fiber bulk laxatives • Insoluble-fiber bulk laxatives  <p><small>T150</small></p>
<p>T151</p>	<p>Wheat Bran and Stool Weight: A Dose Response</p>	<p>Wheat Bran and Stool Weight: A Dose Response</p>  <p>Increase in stool weight over baseline (g)</p> <p>Wheat fiber (g)</p> <p>$P < 0.01$ $N = 6$</p> <p><small>Jenkins DJ et al. Am J Gastro 1987; 82:1259</small></p> <p><small>T151</small></p>

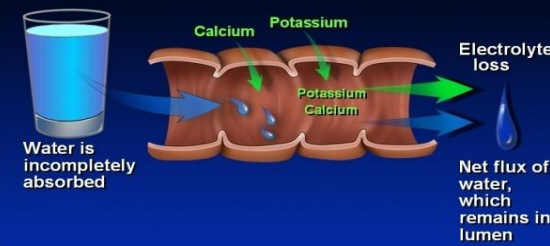
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<p>T152</p>	<p>Stimulant Laxatives: Classification and Mechanism of Action-Slide 1 of 2</p>	<p>Stimulant Laxatives: Classification and Mechanism of Action</p> <ul style="list-style-type: none"> • Anthraquinones (sennosides) • Bisacodyl • Castor oil • Diphenylmethane derivatives  <ul style="list-style-type: none"> • ↓ Absorption • ↑ Motility • ↑ Prostaglandins <p><small>Locke GR III et al. Gastroenterology 2000; 119:1766</small></p> <p><small>T152</small></p>
<p>T153</p>	<p>Stimulant Laxatives: Classification and Mechanism of Action-Slide 2 of 2</p>	<p>Stimulant Laxatives: Classification and Mechanism of Action</p> <ul style="list-style-type: none"> • Anthraquinones (sennosides) • Bisacodyl  <ul style="list-style-type: none"> • Laxative is cleaved by bacteria • Enteric nerves are stimulated <p><small>Locke GR II et al. Gastroenterology 2000; 119:1766</small></p> <p><small>T153</small></p>
<p>T154</p>	<p>Efficacy of Stimulant Laxatives</p>	<p>Efficacy of Stimulant Laxatives</p> <ul style="list-style-type: none"> • 4 randomized comparative trials <ul style="list-style-type: none"> • None placebo-controlled • Low-quality study design • No difference between stimulant laxative and control laxative in stool frequency or consistency • In 1 study <ul style="list-style-type: none"> • Lactulose was superior to the "irritant laxative:" 58% vs 42% were passing a normal stool by day 7 • Insufficient evidence to make a recommendation regarding efficacy <p><small>Brandt LJ et al. Am J Gastroenterol 2005; 100:S5</small></p> <p><small>T154</small></p>

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<p>T155</p>	<p>FDA-Approved Treatment Options for Constipation</p>	<p>FDA-Approved Treatment Options for Constipation</p> <table border="1"> <tr> <td>Osmotic agents</td> <td>Lactulose</td> <td>Indicated for the treatment of constipation</td> </tr> <tr> <td></td> <td>Polyethylene glycol (PEG)</td> <td>Indicated for the short-term treatment of occasional constipation</td> </tr> <tr> <td>5-HT₄ receptor agonist</td> <td>Tegaserod*</td> <td>Indicated for - Men and women < 65 years old with chronic idiopathic constipation - Women with irritable bowel syndrome with constipation <i>*(withdrawn 4/2/08, Emergency IND)</i></td> </tr> <tr> <td>Chloride channel activator</td> <td>Lubiprostone</td> <td>Indicated for chronic idiopathic constipation in adults</td> </tr> </table> <p><small>Physicians' Desk Reference 2005. Montvale, NJ. Thomson PDR; 2005 Cash BD, Lacy BE. Gastroenterol Hepatol. 2006; 2:736</small></p> <p> T155</p>	Osmotic agents	Lactulose	Indicated for the treatment of constipation		Polyethylene glycol (PEG)	Indicated for the short-term treatment of occasional constipation	5-HT ₄ receptor agonist	Tegaserod*	Indicated for - Men and women < 65 years old with chronic idiopathic constipation - Women with irritable bowel syndrome with constipation <i>*(withdrawn 4/2/08, Emergency IND)</i>	Chloride channel activator	Lubiprostone	Indicated for chronic idiopathic constipation in adults
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<p>T156</p>	<p>Osmotic Laxatives: Mono- and Disaccharides-Slide 1 of 2</p>	<p>Osmotic Laxatives: Mono- and Disaccharides</p>  <ul style="list-style-type: none"> • Laxatives metabolized by bacteria . . . <p><small> Bass P, Dennis S. J Clin Gastroenterol. 1981; 3 (Suppl 1):23 Ramkumar D, Rao SS. Am J Gastroenterol. 2005; 100:936</small></p> <p> T156</p>												
<p>T157</p>	<p>Osmotic Laxatives: Mono- and Disaccharides-Slide 2 of 2</p>	<p>Osmotic Laxatives: Mono- and Disaccharides</p>  <ul style="list-style-type: none"> • Laxatives metabolized by bacteria . . . • . . . to short-chain fatty acids, • increasing the osmotic load and changing the pH <p><small> Bass P, Dennis S. J Clin Gastroenterol. 1981; 3 (Suppl 1):23 Ramkumar D, Rao SS. Am J Gastroenterol. 2005; 100:936</small></p> <p> T157</p>												


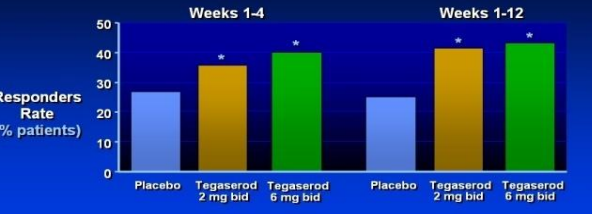
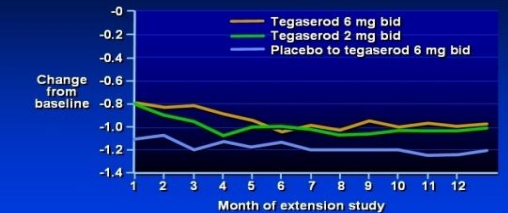
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<p>T158</p>	<p>Osmotic Laxatives: Saline Laxatives</p>	<p>Osmotic Laxatives: Saline Laxatives</p>  <p>Water is incompletely absorbed</p> <p>Calcium Potassium Potassium Calcium</p> <p>Electrolyte loss</p> <p>Net flux of water, which remains in lumen</p> <p>R</p> <p>T158</p>								
<p>T159</p>	<p>Osmotic Laxatives: Classification</p>	<p>Osmotic Laxatives: Classification</p> <ul style="list-style-type: none"> • Poorly absorbed mono- and disaccharides <ul style="list-style-type: none"> • Lactulose • Mannitol • Sorbitol • Glycerin suppositories • Saline laxatives <ul style="list-style-type: none"> • Magnesium: citrate, sulphate, hydroxide • Sodium and disodium phosphate • Other <ul style="list-style-type: none"> • Polyethylene glycol (PEG) <p>R</p> <p>T159</p>								
<p>T160</p>	<p>Effectiveness and Safety Profile of Lactulose</p>	<p>Effectiveness and Safety Profile of Lactulose</p> <table border="1"> <thead> <tr> <th>Studies</th> <th>Summary and Recommendations</th> <th>Adverse Events</th> <th>Pregnancy Category</th> </tr> </thead> <tbody> <tr> <td>3 RPCTs</td> <td>Improves stool frequency and consistency</td> <td>Nausea Vomiting Bloating Flatulence Intestinal cramps</td> <td>B</td> </tr> </tbody> </table> <p><small>RPCT = randomized placebo-controlled trial Brandt LJ et al. Am J Gastroenterol. 2005; 100(suppl 1):S5. Physicians' Desk Reference 2005. Montvale, NJ. Thomson PDR; 2005</small></p> <p>R</p> <p>T160</p>	Studies	Summary and Recommendations	Adverse Events	Pregnancy Category	3 RPCTs	Improves stool frequency and consistency	Nausea Vomiting Bloating Flatulence Intestinal cramps	B
Studies	Summary and Recommendations	Adverse Events	Pregnancy Category							
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<p>T161</p>	<p>Short-Term Effectiveness of PEG 3350 in Chronic Constipation</p>	<p>Short-Term Effectiveness of PEG 3350 in Chronic Constipation</p> <p>No. of BMs / week</p> <p>Legend: Placebo, PEG 3350 (17g)</p> <p>Baseline Week 1 Week 2</p> <p>$P < 0.01$ $P < 0.001$</p> <p>N = 151 (87% female)</p> <p>DiPalma JA et al. Am J Gastroenterol. 2000; 95:446</p> <p>T161</p>								
<p>T162</p>	<p>Long-Term Effectiveness of PEG 3350 in Chronic Constipation</p>	<p>Long-Term Effectiveness of PEG 3350 in Chronic Constipation</p> <p>Successful treatment after 6 months</p> <p>% of patients</p> <p>Legend: PEG, Placebo</p> <p>All n=304 Elderly n=75</p> <p>* $P < 0.001$</p> <p>DiPalma JA et al. Am J Gastroenterol. 2007; 102:1436</p> <p>T162</p>								
<p>T163</p>	<p>Effectiveness and Safety Profile of PEG 3350</p>	<p>Effectiveness and Safety Profile of PEG 3350</p> <table border="1"> <thead> <tr> <th>Studies</th> <th>Summary and Recommendations</th> <th>Adverse Events</th> <th>Pregnancy Category</th> </tr> </thead> <tbody> <tr> <td>5 RCTs</td> <td>Effective at improving stool frequency and consistency</td> <td>Nausea Bloating Cramping</td> <td>C</td> </tr> </tbody> </table> <p>Caution regarding electrolyte disturbances</p> <p>RCTs = randomized controlled trials</p> <p>Brandt LJ et al. Am J Gastroenterol. 2005; 100(suppl 1):S5. Tran LC et al. J Clin Gastroenterol. 2005; 39:600 Physicians' Desk Reference 2005. Montvale, NJ. Thomson PDR; 2005</p> <p>T163</p>	Studies	Summary and Recommendations	Adverse Events	Pregnancy Category	5 RCTs	Effective at improving stool frequency and consistency	Nausea Bloating Cramping	C
Studies	Summary and Recommendations	Adverse Events	Pregnancy Category							
5 RCTs	Effective at improving stool frequency and consistency	Nausea Bloating Cramping	C							

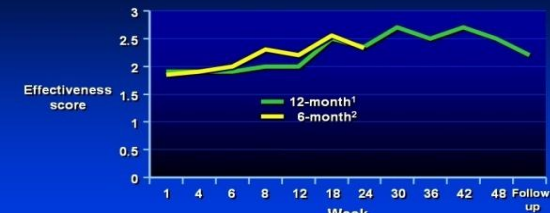
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<p>T164</p>	<p>Serotonin Plays an Important Role in Bowel Function and Sensation</p>	<p>Serotonin Plays an Important Role in Bowel Function and Sensation</p>  <ul style="list-style-type: none"> • Enterochromaffin cells (EC) secrete serotonin into the intestinal wall • Serotonin binds to receptors on nerves to modulate motility, secretion, and sensation • SERT (serotonin reuptake transporter) mediates epithelial cell uptake of serotonin where it is inactivated <p>Nerve terminal Adapted from Gershon MD. <i>Rev Gastrointestinal Dis.</i> 2003; 3(suppl):S25</p> <p>T164</p>																																																				
<p>T165</p>	<p>Complete Spontaneous Bowel Movement Rate with Tegaserod vs Placebo in Chronic Constipation</p>	<p>Complete Spontaneous Bowel Movement Rate with Tegaserod vs Placebo in Chronic Constipation</p>  <table border="1"> <caption>Complete Spontaneous Bowel Movement Rate with Tegaserod vs Placebo in Chronic Constipation</caption> <thead> <tr> <th>Time Period</th> <th>Placebo</th> <th>Tegaserod 2 mg bid</th> <th>Tegaserod 6 mg bid</th> </tr> </thead> <tbody> <tr> <td>Weeks 1-4</td> <td>~28%</td> <td>~38%*</td> <td>~42%*</td> </tr> <tr> <td>Weeks 1-12</td> <td>~26%</td> <td>~42%*</td> <td>~44%*</td> </tr> </tbody> </table> <p>*P < .0001 Responders = Increase of ≥ 1 CSBM/wk and treated for ≥ 7 days. Johanson JF et al. <i>Clin Gastroenterol Hepatol.</i> 2004; 2:796</p> <p>T165</p>	Time Period	Placebo	Tegaserod 2 mg bid	Tegaserod 6 mg bid	Weeks 1-4	~28%	~38%*	~42%*	Weeks 1-12	~26%	~42%*	~44%*																																								
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<p>T166</p>	<p>Sustained Improvement in Chronic Constipation With Tegaserod Over 13 Months</p>	<p>Sustained Improvement in Chronic Constipation With Tegaserod Over 13 Months</p>  <table border="1"> <caption>Sustained Improvement in Chronic Constipation With Tegaserod Over 13 Months</caption> <thead> <tr> <th>Month</th> <th>Tegaserod 6 mg bid</th> <th>Tegaserod 2 mg bid</th> <th>Placebo to tegaserod 6 mg bid</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>2</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>3</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>4</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>5</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>6</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>7</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>8</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>9</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>10</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>11</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> <tr> <td>12</td> <td>-0.8</td> <td>-0.8</td> <td>-1.1</td> </tr> </tbody> </table> <p>Improvements were statistically significant ($P < 0.0001$) with an average improvement of 1 point on a 5-point scale Muller-Lissner S et al. <i>Am J Gastroenterol.</i> 2006; 101:2558</p> <p>T166</p>	Month	Tegaserod 6 mg bid	Tegaserod 2 mg bid	Placebo to tegaserod 6 mg bid	1	-0.8	-0.8	-1.1	2	-0.8	-0.8	-1.1	3	-0.8	-0.8	-1.1	4	-0.8	-0.8	-1.1	5	-0.8	-0.8	-1.1	6	-0.8	-0.8	-1.1	7	-0.8	-0.8	-1.1	8	-0.8	-0.8	-1.1	9	-0.8	-0.8	-1.1	10	-0.8	-0.8	-1.1	11	-0.8	-0.8	-1.1	12	-0.8	-0.8	-1.1
Month	Tegaserod 6 mg bid	Tegaserod 2 mg bid	Placebo to tegaserod 6 mg bid																																																			
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7	-0.8	-0.8	-1.1																																																			
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9	-0.8	-0.8	-1.1																																																			
10	-0.8	-0.8	-1.1																																																			
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<p>T167</p>	<p>Polyethylene Glycol vs Tegaserod in Chronic Constipation</p>	<p>Polyethylene Glycol vs Tegaserod in Chronic Constipation</p> <p>Primary Endpoint = "Successful Treatment:" 50.0% of PEG vs 30.8% of tegaserod patients (P=0.003)</p> <table border="1"> <caption>Secondary Efficacy Criteria</caption> <thead> <tr> <th>Criteria</th> <th>PEG (Mean ±SD)</th> <th>Tegaserod (Mean ±SD)</th> <th>P-value</th> </tr> </thead> <tbody> <tr> <td>BM/week</td> <td>~10</td> <td>~8</td> <td>0.02</td> </tr> <tr> <td>Satisfactory BM/week</td> <td>~7</td> <td>~5</td> <td>0.07</td> </tr> <tr> <td>CSBM</td> <td>~6</td> <td>~4</td> <td>0.16</td> </tr> <tr> <td>Global Assessment</td> <td>~2</td> <td>~1</td> <td>0.08</td> </tr> <tr> <td>Rescue Tablets/week</td> <td>~1</td> <td>~0.5</td> <td>0.03</td> </tr> </tbody> </table> <p>Secondary Efficacy Criteria</p> <p><i>Di Palma JA et al. Am J Gastroenterol. 2007; 102:1964</i></p>	Criteria	PEG (Mean ±SD)	Tegaserod (Mean ±SD)	P-value	BM/week	~10	~8	0.02	Satisfactory BM/week	~7	~5	0.07	CSBM	~6	~4	0.16	Global Assessment	~2	~1	0.08	Rescue Tablets/week	~1	~0.5	0.03
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<p>T168</p>	<p>Chloride Channels in Intestinal Transport</p>	<p>Chloride Channels in Intestinal Transport</p> <p>Enterocytes</p> <p>Tight junction</p> <p>Ion Transport</p> <p><i>Di Palma JA et al. Am J Gastroenterol. 2007; 102:1964</i></p>																								
<p>T169</p>	<p>Effects of Lubiprostone on Number of Spontaneous Bowel Movements</p>	<p>Effects of Lubiprostone on Number of Spontaneous Bowel Movements</p> <table border="1"> <caption>Spontaneous Bowel Movements (SBMs) per week</caption> <thead> <tr> <th>Week</th> <th>24 µg lubiprostone bid (Mean)</th> <th>Placebo (Mean)</th> <th>P-value</th> </tr> </thead> <tbody> <tr> <td>Baseline</td> <td>~1.5</td> <td>~1.5</td> <td>-</td> </tr> <tr> <td>Week 1</td> <td>~5.5</td> <td>~3.5</td> <td>P = 0.0001</td> </tr> <tr> <td>Week 2</td> <td>~5.0</td> <td>~3.0</td> <td>P = 0.0017</td> </tr> <tr> <td>Week 3</td> <td>~5.2</td> <td>~2.8</td> <td>P = 0.0002</td> </tr> <tr> <td>Week 4</td> <td>~5.3</td> <td>~2.9</td> <td>P = 0.0002</td> </tr> </tbody> </table> <p>SBM = spontaneous bowel movements</p> <p><i>Johanson JF et al. Am J Gastroenterol. 2008;103:170.</i></p>	Week	24 µg lubiprostone bid (Mean)	Placebo (Mean)	P-value	Baseline	~1.5	~1.5	-	Week 1	~5.5	~3.5	P = 0.0001	Week 2	~5.0	~3.0	P = 0.0017	Week 3	~5.2	~2.8	P = 0.0002	Week 4	~5.3	~2.9	P = 0.0002
Week	24 µg lubiprostone bid (Mean)	Placebo (Mean)	P-value																							
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<p>T170</p>	<p>Lubiprostone: Global Assessment of Treatment from Open-Label Follow-up Trials</p>	<p>Lubiprostone: Global Assessment of Treatment from Open-Label Follow-up Trials</p>  <p>Effectiveness score</p> <p>Week</p> <p>0=Not at all effective; 1=A little bit effective; 2=Moderately effective; 3=Quite a bit effective; 4=Extremely effective</p> <p>¹ Ueno R et al. Am J Gastroenterol. 2005;101(Suppl):S491 ² Johanson JF et al. Am J Gastroenterol. 2005;100(Suppl):S325</p> <p>T170</p>
<p>T171</p>	<p>Safety Profile of Lubiprostone</p>	<p>Safety Profile of Lubiprostone</p> <ul style="list-style-type: none"> • Most common adverse events were nausea (31%), diarrhea (13%), and headache (13%) • No clinically significant changes in serum electrolyte levels • No drug-drug interactions • Pregnancy category C <p>AMITIZA (lubiprostone) prescribing information. NDA 21-909. Jan 2006 US FDA Web site.</p> <p>T171</p>
<p>T172</p>	<p>Investigational Therapies for Chronic Constipation: Something Old, Something New...</p>	<p>Investigational Therapies for Chronic Constipation: Something Old, Something New...</p> <ul style="list-style-type: none"> • Available Now <ul style="list-style-type: none"> ◦ Colchicine ◦ Misoprostol • In Development <ul style="list-style-type: none"> ◦ Neurotrophin 3 ◦ New serotonergic agents (renzapride) ◦ Guanylate cyclase agonist (linaclotide) ◦ Opiate antagonists (methylnaltrexone) ◦ Motilin agonists (mitemincal) <p>T172</p>

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<p>T173</p>	<p>Effect of Methylnaltrexone* on Opioid-Induced Constipation</p>	
<p>T174</p>	<p>Biofeedback: EMG or Pressure Sensors</p>	
<p>T175</p>	<p>Effects of Biofeedback on Dyssynergic Defecation</p>	<ul style="list-style-type: none"> • Baseline intrarectal and anal sphincter pressures • Improved pushing • Paradoxical contraction remains • Coordinated relaxation • Increased intrarectal pressure • Relaxation in anal sphincter <p>Rao SSC. Gastroenterol Clin North Am. 2003;32:659</p>


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<p>T176</p>	<p>Biofeedback Improves Dyssynergic Defecation: Results from a Controlled Trial</p>	<p>Biofeedback Improves Dyssynergic Defecation: Results from a Controlled Trial</p> <p>Satisfactory Ratings at 6 Months</p> <table border="1"> <caption>Satisfactory Ratings at 6 Months</caption> <thead> <tr> <th>Rating</th> <th>Laxatives (%)</th> <th>Biofeedback (%)</th> </tr> </thead> <tbody> <tr> <td>Worse</td> <td>~10</td> <td>~5</td> </tr> <tr> <td>No Change</td> <td>~50</td> <td>~15</td> </tr> <tr> <td>Fair</td> <td>~20</td> <td>~10</td> </tr> <tr> <td>Major</td> <td>~20</td> <td>~80</td> </tr> </tbody> </table> <p>Chiaroni G et al. <i>Gastroenterology</i> 2006; 130:657</p> <p>T176</p>	Rating	Laxatives (%)	Biofeedback (%)	Worse	~10	~5	No Change	~50	~15	Fair	~20	~10	Major	~20	~80
Rating	Laxatives (%)	Biofeedback (%)															
Worse	~10	~5															
No Change	~50	~15															
Fair	~20	~10															
Major	~20	~80															
<p>T177</p>	<p>Biofeedback for Dyssynergic Defecation</p>	<p>Biofeedback for Dyssynergic Defecation</p> <p>Standard Therapy: N=24 (22 F), Biofeedback: N= 28 (25 F), Sham Biofeedback: N=25 (23 F)</p> <table border="1"> <caption>CSBMs/week (mean + SEM)</caption> <thead> <tr> <th>Treatment</th> <th>Baseline</th> <th>Posttherapy</th> </tr> </thead> <tbody> <tr> <td>Biofeedback</td> <td>~2.1</td> <td>~3.9</td> </tr> <tr> <td>Sham biofeedback</td> <td>~1.2</td> <td>~2.3</td> </tr> <tr> <td>Standard</td> <td>~1.4</td> <td>~1.6</td> </tr> </tbody> </table> <p>* P<.02 vs baseline ** P<.05 vs sham *** P<.006 vs standard</p> <p>Rao SSC et al. <i>Clin. Gastroenterol. Hepatol.</i> 2007; 5:331</p> <p>T177</p>	Treatment	Baseline	Posttherapy	Biofeedback	~2.1	~3.9	Sham biofeedback	~1.2	~2.3	Standard	~1.4	~1.6			
Treatment	Baseline	Posttherapy															
Biofeedback	~2.1	~3.9															
Sham biofeedback	~1.2	~2.3															
Standard	~1.4	~1.6															
<p>T178</p>	<p>Comorbid Psychological (PD) and Eating (ED) Disorders Reduce the Efficacy of Pelvic Floor Biofeedback</p>	<p>Comorbid Psychological (PD) and Eating (ED) Disorders Reduce the Efficacy of Pelvic Floor Biofeedback</p> <table border="1"> <caption>Outcome % of patients</caption> <thead> <tr> <th>Group</th> <th>Improvement (%)</th> <th>No Improvement (%)</th> </tr> </thead> <tbody> <tr> <td>Without PD</td> <td>~85</td> <td>~15</td> </tr> <tr> <td>PD Without ED</td> <td>~75</td> <td>~25</td> </tr> <tr> <td>PD With ED</td> <td>~55</td> <td>~45</td> </tr> </tbody> </table> <p>Association between psychological disorder and outcome at 2 weeks; P=0.03</p> <p>Nehra V et al. <i>Am J Gastroenterol.</i> 2000; 95:1755</p> <p>T178</p>	Group	Improvement (%)	No Improvement (%)	Without PD	~85	~15	PD Without ED	~75	~25	PD With ED	~55	~45			
Group	Improvement (%)	No Improvement (%)															
Without PD	~85	~15															
PD Without ED	~75	~25															
PD With ED	~55	~45															

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<p>T179</p>	<p>Colectomy for Refractory Slow-Transit Constipation</p>	<p>Colectomy for Refractory Slow-Transit Constipation</p> <table border="1"> <thead> <tr> <th>Approach</th> <th>Indication</th> <th>Outcomes</th> </tr> </thead> <tbody> <tr> <td>Total colectomy + ileorectal anastomosis</td> <td>Medically refractory slow-transit constipation without dysynergic defecation</td> <td>Review of 32 studies Satisfaction: 39-100%</td> </tr> <tr> <td></td> <td></td> <td><i>All studies were uncontrolled with small sample sizes and variable outcome measures</i></td> </tr> <tr> <td></td> <td></td> <td>Most common complications Small-bowel obstruction, diarrhea, incontinence</td> </tr> <tr> <td></td> <td></td> <td>Predictors of poor outcome Patients with upper gut dysmotility (gastroparesis, pseudo-obstruction) Psychological disturbances</td> </tr> </tbody> </table> <p><small>Knowles CH et al. Ann Surg, 1999; 230:627</small></p>	Approach	Indication	Outcomes	Total colectomy + ileorectal anastomosis	Medically refractory slow-transit constipation without dysynergic defecation	Review of 32 studies Satisfaction: 39-100%			<i>All studies were uncontrolled with small sample sizes and variable outcome measures</i>			Most common complications Small-bowel obstruction, diarrhea, incontinence			Predictors of poor outcome Patients with upper gut dysmotility (gastroparesis, pseudo-obstruction) Psychological disturbances
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<p>T180</p>	<p>Section Title: Fecal Incontinence</p>																
<p>T181</p>	<p>Treatment of Fecal Incontinence</p>	<p>Treatment of Fecal Incontinence</p> <p><small>T181</small></p>															
<p>T182</p>	<p>Biofeedback for Fecal Incontinence: Training Methods</p>	<p>Biofeedback for Fecal Incontinence: Training Methods</p> <p><small>T182</small></p>															

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T183	Surgical Approaches for Fecal Incontinence	<p style="text-align: center;">Surgical Approaches for Fecal Incontinence</p> <table border="1"><thead><tr><th>Approach</th><th>Short-Term Results</th><th>Long-Term Results</th></tr></thead><tbody><tr><td>Anterior sphincteroplasty</td><td>Improved continence in 85% of those with sphincter defects</td><td>Failure rates of 50% after 40-60 months</td></tr><tr><td>Colostomy</td><td></td><td>Reserve for only the most severe cases</td></tr></tbody></table> <p> T183</p>	Approach	Short-Term Results	Long-Term Results	Anterior sphincteroplasty	Improved continence in 85% of those with sphincter defects	Failure rates of 50% after 40-60 months	Colostomy		Reserve for only the most severe cases
Approach	Short-Term Results	Long-Term Results									
Anterior sphincteroplasty	Improved continence in 85% of those with sphincter defects	Failure rates of 50% after 40-60 months									
Colostomy		Reserve for only the most severe cases									