Introduction

Irritable bowel syndrome (IBS) is a common disorder characterised by abdominal pain associated with abnormal bowel movement without any clinically identifiable structural or biochemical abnormality. It is a famous “heart sinker” for both patients and doctors partly because of the poor understanding of the disease by both parties, thus creating opportunities for communication problems during the consultation process. This article aims to highlight some of the new findings in IBS.

Diagnosis

Since IBS has no characteristic pathophysiological abnormality, the diagnosis is mainly based on symptom analysis. Common differential diagnoses include drug induced GI side effects, carcinoma of colon, thyrotoxicosis, parasitic infestation and inflammatory bowel disease. Alarming symptoms and signs such as blood in stool, pallor, fever, weight loss, presence of abdominal mass should be looked for and their presence will prompt for further investigations to look for an organic lesion. The Hong Kong Society of Gastrointestinal Motility puts forward an algorithm for management as shown in flowchart 1.

The Manning criteria (Table 1) are commonly used for diagnosis for decades. In an attempt to select a more homogeneous group of patients for various purposes, the International Working Party on Functional GI Disorder first proposed the Rome I criteria in 1989 and subsequently Rome II criteria in 1999 (Table 2). Functional bowel disorders are sub-classified into IBS, functional constipation, functional diarrhoea, functional abdominal bloating and functional abdominal pain syndrome, basing on a detail analysis of symptoms. Abdominal pain or discomfort is an essential feature to distinguish IBS from functional diarrhoea or constipation. The pain or discomfort has to occur continuously or intermittently in 12 weeks out of the past 1 year and the pain is associated with altered bowel habits. There has also been a proposed classification to distinguish between diarrhoea predominant IBS and constipation predominant IBS (Table 3).

Table 1. Manning Criteria (1978)

| Abdominal pain eased after bowel movement |
| Looser stools at onset of pain |
| More frequent bowel movements at onset of pain |
| Abdominal distension |
| Mucus per rectum |
| Feeling of incomplete emptying |

Table 2. Rome II Criteria (1999)

Main Diagnostic Criteria : 2 out of 3
>12 weeks in the past 12 months of abdominal pain or discomfort
1. Relief with defecation
2. Onset of pain or discomfort associated with change of frequency of stool
3. Onset of pain or discomfort associated with change of form of stool
### Table 3  Different Types of IBS Patients (Rome II)

<table>
<thead>
<tr>
<th>Type of IBS</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Diarrhoea Predominant IBS (D-IBS)</td>
<td>Usual frequency of stool more than 3 times per day</td>
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<tr>
<td></td>
<td>OR usual form of stool is loose</td>
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<tr>
<td></td>
<td>AND not hard</td>
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<td></td>
<td>OR frequently feel the sense of urgency</td>
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<td></td>
<td>AND do not feel straining to defecate</td>
</tr>
<tr>
<td>Constipation Predominant IBS (C-IBS)</td>
<td>Usual frequency of stool &lt; 3 times per week</td>
</tr>
<tr>
<td></td>
<td>OR usual form of stool is hard</td>
</tr>
<tr>
<td></td>
<td>AND not loose</td>
</tr>
<tr>
<td></td>
<td>Or always feel straining to defecate</td>
</tr>
<tr>
<td></td>
<td>AND do not frequently feel the sense of urgency</td>
</tr>
<tr>
<td>Non-specific IBS</td>
<td>Those who do not fulfill the above criteria</td>
</tr>
<tr>
<td></td>
<td>i.e. neither Diarrhoea nor Constipation Predominant IBS</td>
</tr>
</tbody>
</table>

### Flowchart 1: Diagnostic Algorithm of IBS

1. Abdominal pain and altered bowel habit
2. Detail history and examination

- 1. Frequent abdominal pain (on average, ≥ 1 attack/month, fluctuating course)
- 2. Relief of abdominal pain after defaecation
- 3. Loose or harder stool with onset of abdominal pain
- 4. Altered bowel frequency with onset of abdominal pain
- 5. Abdominal distension
- 6. Passage of mucus per rectum
- 7. Sensation of incomplete evacuation

Any alarm features such as:
- bleeding per rectum
- steatorrhoea
- weight loss
- fever
- nocturnal symptoms
- onset at age ≥ 40
- recent onset
- progressive course
- family history of colon cancer (especially at young age)
- abnormal sign on examination

- IBS more likely

Simple investigations:
- Full blood counts
- Erythrocyte sedimentation rate
- Thyroid function test
- Stool occult blood, leukocytes, culture, ova and cyst
- Sigmoidoscopy

- Any investigation results normal

Review diagnosis in 6 to 12 weeks, if no improvement with treatment, consider referral to specialist

### Organic GI disease

- Investigate along the line of organic GI disease

Any alarm features such as:
- bleeding per rectum
- steatorrhoea
- weight loss
- fever
- nocturnal symptoms
- onset at age ≥ 40
- recent onset
- progressive course
- family history of colon cancer (especially at young age)
- abnormal sign on examination

- Investigation results abnormal

- Organic GI disease
New Insights in Pathophysiology

The past several years have seen a surge in activities aiming at better understanding and more effective treatment for IBS. Classical aetiologies have implicated psychosocial factors and abnormalities in gastrointestinal motility. The new model is based on a more comprehensive approach encompassing alterations within the central nervous system to manifest as altered neuroendocrine responses to stress, altered autonomic input to the gut and alterations in the central processing or modulations of visceral sensory information. The emerging model can explain alterations in bowel habits (autonomic dysregulation), abdominal pain (enhanced visceral sensitivity) and a variety of constitutional symptoms (e.g., malaise). Over the last decade, the role of enhanced visceral sensitivity in the pathophysiology of irritable bowel syndrome has been largely recognised. IBS patients reported pain earlier when a balloon was inflated in the lumen of the bowel as compared with normal controls. New insights have been obtained in the pain sensitivity of human digestive system since the use of electronic barostats for distension studies. These barostats could measure the threshold of pressure and volume inside a distending device that produced discomfort, pain or symptoms such as bloating or rectal urgency. In about 20 human studies comparing healthy controls with IBS patients, two thirds of the patients exhibited a 20%-25% decreased pain threshold to colonic distension. Visceral hypersensitivity could be caused by pathology in the enteric nervous system, spinal reflexes or central nervous system. New brain imaging methods like PET and functional MRI scans have shown that in subgroups of IBS patients there are differences in regions of brain activation, namely the anterior cingulate cortex and associated limbic structure, as compared with controls when visceral pain is induced. These areas in the brain have also been related to psychosocial disturbances like emotional disturbances and stress in other studies. These data thus provide evidence to support the clinical observation of the association among psychological distress, IBS and pain perception. Further research in this field is promising to look into the exact role and impact of acute and chronic stress on the biological aspects of the brain gut axis.

Another exciting area is the recognition that an acute GI infection is a triggering factor for symptom development in a subset of patients with IBS (post-infectious IBS). Increase in intestinal permeability and increase in inflammatory cells and cytokines are observed in this subgroup of patients, which may subsequently lead to visceral hypersensitivity. An attempt to reduce inflammation by systemic steroids or antibiotics has failed to improve symptoms. Alterations in small bowel permeability have been described in this form of IBS. In addition, there are studies that look into some novel areas like alteration of microflora in the GI tract and genetic factors to try to gain a better understanding of the disease nature and, hopefully, the treatment of IBS patients.

Treatment

The conventional approach to the management of IBS patients is summarised in table 6. Some of the published new drug studies are highlighted.

A. 5-Hydroxytryptamine (5-HT) -4 agonists and 5-HT3 antagonists:

Tegaserod is now available in clinical practice and is indicated for female patients with C-IBS and functional constipation. It is a 5-HT4 receptor agonist that stimulates the smooth muscle in the GI tract, increases peristalsis and accelerates the gut transit time. Randomised double blind placebo controlled studies have shown that tegaserod 12mg/day is superior to placebo in improving global symptoms in C-IBS patients. The therapeutic gain over placebo ranges from 5-20% in these studies. The most frequent side effects are transient diarrhoea, headache and abdominal pain and full response is expected after 4-6 weeks of treatment. It is contraindicated in patients with significant cardiac, liver or renal diseases. Recently another 5-HT4 agonist renzapride also appears to be promising.

The effects of 5-HT3 antagonists on the sensitivity of the lower gut have been extensively investigated. Randomised trials have shown that both alosetron and cilansetron are more effective than placebo in treating D-IBS patients. However the rare side effects of severe ischaemic colitis have raised safety concerns in USA and alosetron is not available in HK. In general, there are reports of ischaemic colitis in patients with IBS in post-marketing survey. A causal relationship between ischaemic colitis and alosetron or tegaserod has not been confirmed but close monitoring of patients taking these drugs is recommended. Patients should be educated about the alarm features of ischaemic colitis such as blood in stool or worsening abdominal pain to facilitate early recognition of this potentially life-threatening condition.

B. Antidepressants :

One approach is the use of low dose antidepressants (e.g., Amtriptyline 10-75 mg at bedtime, Imipramine 10-75 mg at bedtime) for moderate to severe pains that are poorly controlled by antispasmodics. They have neuromodulatory and analgesic properties independent of their psychotropic effects. They may aggravate constipation and therefore it is more suitable for diarrhoea-predominant IBS. Beneficial effect may not be apparent until 6 to 8 weeks later. Selective serotonin reuptake inhibitors (SSRIs) (e.g., Fluoxetine, Paroxetine, Sertraline) have fewer side effects, faster onset and better safety profile. It is useful for treatment of IBS patients with concomitant anxiety or depressive disorders. SSRIs tend to cause diarrhoea instead of constipation and therefore they may be suitable for constipation-predominant IBS. Their efficacy in pain relief is, however, less well defined. Patient should be explained clearly the rationale of using anti-depressants to avoid unnecessary fear of psychiatric illness.
C. Probiotics and antibiotics:
Probiotics or non-absorbable antibiotic (lactobacilli, bifidobacteria, VSL#3 and rifaximin) have been tried in IBS to try to alter the intestinal micro-flora, hopefully to reduce visceral hypersensitivity. The improvement for global symptom control is controversial but individual symptoms like bloating, flatulence or pain may respond. Confirmatory studies in the future are awaited. Furthermore, one recent study has suggested that rifaximin may be effective in the prevention of post-infectious IBS.

D. Herbal medicine:
Well conducted trials from Australia and Germany have shown that specific types of herbal medicine significantly improved symptom scores when compared to placebo group. The underlying mechanism is, however, uncertain as there are numerous components in the herbal medicine and further studies are awaited.

Table 6. Conventional approach to the management of IBS patients

1. General measures, e.g. Explanation of mechanisms of symptom production, reassurance
2. Exclusion diet, e.g. dairy products, coffee
3. Soluble fibre supplement or laxatives for constipation
4. Anti-diarrhoeal agents for diarrhoea, e.g. loperamide
5. Antispasmodic agents for pain, e.g. mebeverine, hyoscine methobromide, octilonium bromide

Conclusion
New concepts on the pathophysiology of IBS are based on abnormalities in the central and autonomic nervous system and visceral hypersensitivity. Emerging new mechanisms of both peripheral and central origin have shown that IBS is actually a very heterogeneous condition. Advances in the field are exciting and hopefully would lead to improvement in the management of IBS patients.

MCHK CME Programme Self-assessment Questions
Please read the article entitled "Irritable Bowel Syndrome - A Syndrome in Evolution" by Dr. Ambrose CP Kwan and Dr. Thomas ST Lai and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheet via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 December 2005. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please choose the best answer.

1. The following is not true about the diagnosis of IBS:
A. Abdominal pain or discomfort must be present according to the Rome criteria
B. Bowel symptoms like straining or urgency are not absolute criteria for the diagnosis of IBS in Rome II criteria
C. Patients with symptoms fulfilling Rome I criteria had a > 95% chance of having IBS
D. Patients with IBS often had symptoms of dyspepsia or GERD.
E. None of the above

2. The following is not true about sub-classification of IBS:
A. Alternating type is difficult to define
B. Sub-classification is of no clinical value.
C. Mucus and abdominal distension are not discriminating symptoms
D. Stool forms in the Bristol stool form scale correlates with transit time
E. None of the above

3. The following are keys to treatment of IBS
A. Education of patients about IBS
B. Dietary modification
C. Focus on health
D. Pharmacotherapy of GI symptoms
E. All of the above

4. The following diseases were considered as differential diagnoses of patients with IBS:
A. Thyrotoxicosis
B. Malabsorption syndrome
C. Carcinoma of colon
D. Inflammatory bowel disorders
E. All of the above

5. Which one of the following was not considered as an alarming signs or symptoms of IBS?
A. Pallor
B. Weight loss
C. Severe abdominal pain
D. Fever
E. Blood in stool
6. Which one of the following non-GI symptoms is not associated with IBS?
A. Malaise
B. Muscle pain
C. Dyspareunia
D. Frequent urination
E. All of the above

7. Which one of the following is not correct?
A. According to the Rome II criteria, patients with abdominal distension without associated bowel disturbance are considered to have functional abdominal bloating.
B. Bloating usually responds to fibre supplement
C. Anti-cholinergic drugs may worsen symptoms of patients with alternating type of IBS.
D. Laxatives might worsen abdominal pain in patients with constipation predominant IBS.
E. Visceral hypersensitivity is a widely accepted pathophysiology for IBS.

8. Which of the following groups of drugs are being studied for treatment of IBS?
A. Anti-depressants
B. 5-hydroxytryptamine type 4 receptor agonists
C. Herbal medicine
D. Probiotics
E. All of the above

9. Which of the following about tegaserod is not correct:
A. It is a 5-HT4 receptor agonist.
B. It is better than placebo in improving abdominal pain and bowel frequency in patients with C-IBS.
C. Effect of treatment starts to be seen at the end of 4 weeks.
D. Tegaserod has no significant drug interaction with oral contraceptive pills.
E. Diarrhoea is the major side effect.

10. The followings are considered pathophysiological mechanisms of IBS:
A. Brain-gut axis abnormalities
B. Visceral hypersensitivity
C. Psycho-social factors
D. Post-infectious (after an episode of acute bacterial gastroenteritis)
E. All of the above

ANSWER SHEET FOR DECEMBER 2005

Please return the completed answer sheet to the Federation Secretariat on or before 31 December 2005 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Irritable Bowel Syndrome - A Syndrome in Evolution
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Answers to November 2005 issue

Management of Molluscum Contagiosum in Children