Article

SUMMARY

Irritable bowel syndrome is one of the most common reasons for disability and health care seeking. A sensible strategy for management incorporates a confident diagnosis based upon history, physical examination, and pertinent tests. The physician can then reassure the patient, offer dietary and stress management advice, and recommend bran to relieve constipation and to evoke the placebo response. Patients who do not respond could require supportive psychotherapy or a drug for the dominant symptom. A few require careful referral, but overall responsibility should remain with the primary physician.

RÉSUMÉ

Le syndrome du côlon irritable est l'un des motifs les plus courants de consultation et d'incapacité. Après avoir établi un diagnostic probabiliste basé sur l'interrogatoire, l'examen physique et les examens complémentaires appropriés, on abordera le traitement par une attitude de sympathie. Le médecin peut alors rassurer le patient, offrir des conseils diététiques, des conseils permettant un meilleur contrôle du stress psychologique et recommander l'ingestion de son pour soulager la constipation et évoquer une réponse placebo. Quant aux malades réfractaires, ils peuvent nécessiter une psychothérapie de soutien ou un médicament pour atténuer le symptôme dominant. Quelques rares malades nécessiteront une consultation spécialisée mais la responsabilité globale devrait demeurer entre les mains du médecin de première ligne.

Can Farm Physician 1994;40:307-316.

Irritable bowel syndrome

Strategy for the family physician

W. GRANT THOMPSON, MD

RRITABLE BOWEL SYNDROME (IBS) is the most common condition encountered by gastroenterologists. It is also common in family practice and is an important cause of disability and time off work. This article offers a strategy by which family physicians can satisfactorily manage most IBS patients and by which referral to

specialists can be limited to those few

patients with special problems.

Definitions

The IBS is one of the functional gastrointestinal disorders, which are defined as: a variable combination of persistent or recurrent gastrointestinal symptoms not explained by structural or biochemical abnormalities. They include symptoms attributed to the oropharynx, oesophagus, stomach and biliary tree, small and large intestines or anorectum.²

Functional gastrointestinal disorders are listed in *Table 1*. Criteria for diagnosing IBS are found in *Table 2*. Note that other syndromes, such as functional constipation, dyspepsia, or functional diarrhea, are excluded by these criteria because they raise distinct diagnostic and therapeutic issues. Nevertheless, many of the strategies

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proposed here apply to managing these other syndromes.

Minimizing health care use

As the first medical contact of a person complaining of IBS symptoms, a family practitioner is uniquely positioned to ensure the effective employment of health care resources. Patients with IBS have chronic symptoms. Through repeated investigations and ineffective treatments, a few become a costly burden. Early, firm diagnosis, prompt reassurance, and time spent discussing issues surrounding IBS can pay off in the long run through a satisfied patient, secure in the diagnosis, with a realistic view of prognosis.

Global view

The IBS affects 10% to 20% of adults in developed countries.³⁻⁶ The figure is 30% to 40% if all functional gastrointestinal syndromes are included. This is not a disease of modern industrialized culture. It was recognized before the industrial revolution,^{7,8} and a Chinese survey discovered a prevalence similar to that in Western countries.⁹ Epidemiologic surveys report that less than half of the subjects had seen a physician for their IBS complaints. This begs the question, "Why do some people with these common complaints seek help?" An obvious possibility is the severity of the symptoms, especially pain.

Table 1. Classification of functional gastrointestinal disorders

A. FUNCTIONAL ESOPHAGEAL DISORDERS

- A.1 Globus
- A.2 Rumination syndrome
- A.3 Functional chest pain of presumed esophageal origin
- A.4 Functional heartburn
- A.5 Unspecified functional esophageal disorder

B. FUNCTIONAL GASTRODUODENAL DISORDERS

- B.1 Functional (nonulcer) dyspepsia
- **B.2** Aerophagia

C. FUNCTIONAL BOWEL DISORDERS C.1 Irritable bowel

- syndrome
- C.2 Functional abdominal bloating
- C.3 Functional constipation
- C.4 Functional diarrhea
- C.5 Unspecified functional bowel disorder

D. FUNCTIONAL ABDOMINAL PAIN

- D.1 Functional abdominal pain syndrome
- D.2 Unspecified functional abdominal pain

E. FUNCTIONAL BILIARY PAIN

F. FUNCTIONAL ANORECTAL DISORDERS

- F.1 Functional incontinence F.2 Functional anorectal pain
 - F.2A Levator syndrome
 - F.2B Proctalgia fugax
- F.3 Pelvic floor dyssynergia F.4 Unspecified functional
- F.4 Unspecified functiona anorectal disorder

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However, this might not be the only, nor the most important, reason.

In Europe and America, women are twice as likely as men to have IBS and constitute 75% to 80% of IBS patients in clinical practice. 10,11 If we conclude from this that women have more severe IBS, how do we explain the situation in India where men are more likely to bring their IBS complaints to a physician? 12,13 In tertiary care centres (where such things are studied), psychologic problems, such as anxiety, depression, or panic, are more common in IBS patients than others. 14-16 Yet, in the general population, those with IBS who do not seek health care have a psychosocial and personality makeup similar to those without symptoms. 17,18 Furthermore, the reporting of IBS to a physician is commonly preceded by a threatening life event: a death in the family, a loss of job, or marital dissolution. 19,20

It is possible that these confounding factors are the real reason that some patients seek help. Perhaps such a "hidden agenda" underlies the socially acceptable use of gut symptoms as a vehicle for care.

Consider a man who has suffered IBS symptoms all his adult life. Suddenly, his father is found to have carcinoma of the colon. The gut symptoms assume new meaning. Here treatment strategy is obvious. Assure him that he harbours no cancer, and he is unlikely to consult again (except for regular colon cancer surveillance). Someone else, with anxiety or depression, could consciously or subconsciously choose to seek care for IBS symptoms rather than suffer the indignity of admitting to psychosocial distress. For another patient, psychosocial problems could impair his or her ability to cope with symptoms that normally would cause little grief. Yet another might employ symptoms for secondary gain: to manipulate a boss, a spouse, a parent, or a disability insurance adjuster.

Such illness behaviour tends to occur in people who regard colds and other minor illnesses more seriously than usual or who received gifts or a day off school when ill as children.²¹ Probably, most primary care patients have none of these problems and will be satisfied if the somatic symptoms are addressed. However, psychosocial issues are likely to be important in

refractory cases and must be considered in the management plan.

Thus any global view must consider the vast numbers of people with IBS (perhaps 3 million in Canada). Most of those that come to doctors should be manageable at the primary care level if one is able to be firm about the diagnosis, sanguine about the prognosis, and aware of the possibility of a hidden agenda.

Pathogenesis

The belief that IBS is caused by gut spasm was evident as early as 1830 when one author described it as a "spasmodic constriction of the colon."8 This notion has been perpetuated by such obsolete terms as "spastic mucus colitis" or "spastic colon," but has little foundation in science. Attempts to measure colon motility²² and electrical²³ activity have failed to identify physiologic events that are sufficiently sensitive or specific to act as diagnostic markers of IBS. We simply do not understand the mechanisms by which the symptoms are generated. Pharmaceutical advertisements that imply that IBS symptoms are relieved by drugs that reduce gut spasm are unfounded. It is true that, as a group, IBS patients have guts that are more sensitive to distention,24 stress,25 drugs,26 eating,23 and other environmental influences, but it does not follow that any known drug reduces that sensitivity in a meaningful way.

Indeed the pain of IBS could be caused as much by altered perception of events in the gut as by disordered gut function itself.²⁷ The protean manifestations of IBS are unlikely to be due to an underactive or overactive neurotransmitter among the myriad found in the enteric nervous system. Thus a single, pharmacologic quick fix aimed at a possibly errant neuroreceptor seems remote, even fanciful.

Diagnostic strategy

Diagnostic insecurity is the enemy of rational management of IBS. 28-30 Physician insecurity breeds overinvestigation. If a doctor believes that IBS is diagnosed by exclusion, it follows that he or she must prove normality of every abdominal organ: an expensive and unnerving conclusion. Patient insecurity feeds on the notion that something could

have been missed. Relief is at hand if only the doctors could find the trouble! The inevitable outcomes of diagnostic dithering are doctor shopping, demands for referral, and experiments with alternative medicine. ^{31,32}

Physician and patient insecurity can be minimized through a more positive attitude to diagnosis. This implies a careful history to elicit the features of IBS outlined in Table 2. Abdominal pain is a central feature. It occurs anywhere in the abdomen, is often crampy, but most importantly is associated in some way with defecation. A bowel movement can relieve pain, or pain is followed by a change in the frequency and consistency of the stool.^{2,33} In addition there must be an indication of altered defecation with changes in frequency, consistency, or passage of stool, often with mucus and a sensation of abdominal distention. Taken together, these IBS symptoms are not those of cancer or inflammatory bowel disease.

Naturally, when an affliction affects so many people, there will occasionally be coincidental disease. Thus one must carefully inquire after symptoms that suggest anatomic origin, such as fever, bleeding, anemia, weight loss, nocturnal occurrence, or recent onset. Such symptoms are not explained by IBS and require investigation in their own right. No physical findings are attributable to IBS. Most physicians would be further reassured by a normal hemoglobin level, white blood count, and erythrocyte sedimentation rate. Some colon examination seems appropriate also, as much for reassuring the patient as for finding positive results. A gastroenterologist would use fibreoptic sigmoidoscopy. In family practice, proctoscopy or digital rectal examination can suffice.

Special circumstances require special tests.² If a patient is older than 40, has recent onset of symptoms, or has a family history of colon neoplasia, a full colon examination is advisable. In primary care, this is best accomplished through a barium enema, provided that the physician insists on an air-contrast technique that will detect polyps (Figure 1). The symptoms described above are not those of colon cancer, but assurance of a "clean colon" makes sense for such patients

when starting treatment. If there is a family history of inflammatory bowel disease, a small bowel enema and a proctoscopic procedure could be indicated.

Should the patient have been in an area where giardiasis is common, such as the Rocky Mountains, stools should be sent for examination for these organisms. The stool test unfortunately has only about 50% sensitivity. Non-European people could be lactose intolerant. A trial of a milk-free diet is probably more sensible than laboratory testing. For most patients, these tests are unnecessary.

Physicians should inquire after other factors that might exacerbate the symptoms. The excessive use of artificial sugars found in diet gums (sorbitol, mannitol) can have a laxative effect.³⁴ Many drugs given for other purposes affect the gut, and a surprising number of people use laxatives.³⁵ If diarrhea is prominent, the urine should be screened for laxatives. Antibiotics sometimes initiate diarrhea, in some cases a full-blown pseudomembranous colitis. If in doubt, stool should be examined for the Clostridium difficile toxin. Caffeine can be a factor in coffee addicts. Some cannot tolerate gassy vegetables, such as beans or cabbage.

These items do not cause IBS, but they can increase the symptoms and confuse treatment. Although a patient might be convinced he or she is allergic to some foods – and some fringe practitioners foster that belief – there is very little supporting evidence. ³⁶⁻⁴⁰ We humans are suggestible and what we ate at the time symptoms began can become a lifetime scapegoat.

The hidden agenda must be considered in any therapeutic strategy. The real reason for the visit to the doctor can be an important clue to therapy. Fear of disease, concurrent life stress, family strife, or disability issues are all important data. One must also attempt to detect depression, anxiety, or panic that impair one's ability to cope with any symptoms, not just those of IBS.

Treatment strategy Explanation and reassurance.

Armed with a confident diagnosis, and one or two pertinent normal test findings, a physician is in position to reassure the patient. This reassurance can be the most

Table 2. Rome diagnostic criteria for the irritable bowel:

Patients must have both abdominal pain or discomfort and at least two other symptoms.

Patients must have at least 3 months of continuous or recurrent symptoms of abdominal pain or discomfort that is:

- relieved with defecation,
- associated with a change in the frequency of stool, or
- associated with a change in the consistency of stool

AND

Two or more of the following, at least 25% of occasions or days:

- altered stool frequency,
- altered stool **form** (lumpy and hard or loose and watery stool),
- altered stool passage (straining, urgency, or feeling of incomplete evacuation),
- passage of mucus, and
- bloating, or feeling of abdominal distention

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Figure 1. Air-contrast barium enema: If a patient is known to have risk factors for colon cancer and is older than 40 years, an air-contrast barium enema is useful to determine at the outset that the colon is normal.

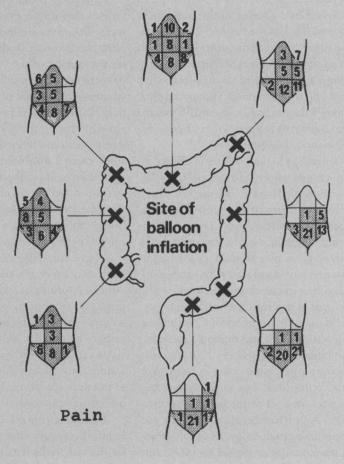


Figure 2. Pain corresponding to site of balloon inflation: Many patients with IBS feel pain when a balloon is inflated at various levels of the gut. Also, IBS patients experience pain and when the balloon is inflated to a lower volume than that observed by control subjects.

effective therapeutic weapon, and the sooner it is deployed the better. One should begin by explaining that the symptoms are common. The good news is that they are themselves benign and do not carry any increased risk of other disease. There are some things the patient can do to help. The not-so-good news is that IBS is chronic, and because the cause is unknown, there is no cure. 41-43

A drawing of the gut helps the doctor explain the location of the pain and indi-

cate the complexity of gut movements required to pass a stool. The marvel is how well the gut works most of the time.

For many patients with IBS, pain can be reproduced experimentally by inflating a balloon at various levels of the gut (Figure 2).⁴⁴ The pain can be said to be due to stretching of the gut, but this is clearly an oversimplification. Patients with IBS also seem to experience pain when the balloon is inflated to a lower volume than other patients feel.²⁴ Occasionally

patients' pain is reproduced by distention during sigmoidoscopy.

It is useful to compare the pain to that of a headache. Very real pain can emanate from the head or gut without any recognizable abnormality of structure or function to explain it. No one doubts the validity of the pain, but its cause is currently beyond medical science. According to the patient's fears, the absence of cancer, inflammatory bowel disease, or other serious affliction must be emphasized.

Counseling. It is difficult to prove that careful attention to an IBS patient's complaints and personal problems is therapeutic. However, evidence⁴⁵ suggests that several brief psychotherapy or support counseling sessions early in the course of the disease lead to greater improvement in symptoms, more satisfaction with care, and quicker return to normal activities. Of greater importance, this improvement, when compared with that of a control group, is sustained 1 year after this extra effort. The authors of this study⁴⁵ point out that the psychotherapy required is within the capability of any concerned physician and centres on confirmation of the diagnosis, reassurance, and discussion of problems in the patient's life.

Another study arrived at similar conclusions, but suggested that success was most likely if the pain was not constant and there was evidence of depression. 46 Thus, authoritative, early attention to a patient with IBS can have lasting benefit. Some counseling and supportive psychotherapy should be part of every therapeutic encounter, but must obviously be tailored to the needs of the patient.

Dietary fibre. Most physicians continue to recommend bran for IBS.⁴⁷ It is true that proof of efficacy has not been established.⁴⁸ Nevertheless, bran or other fibre is useful for most types of constipation, especially that associated with IBS. Furthermore, control groups in fibre trials had a placebo response of 50% to 70%. At the very least, fibre is a safe, cheap way to elicit a placebo response, and reducing constipation could better regulate gut function.

The most common reason for failure of a high-fibre diet is an insufficient dose.

To better monitor progress, a tablespoonful (approximately 15 mL) of bran can be taken three times daily with meals so that it mixes with intestinal contents. If this is unworkable, a twice or once daily regimen can succeed provided that sufficient fibre is taken to improve defecation. Compliance thus assured, the dose can be adjusted for maximum benefit. Bloating and gas are often attributed to bran but should improve as gut transit improves. The objective is to prevent the constipation, and thereby improve bowel habit.

Table 3. Drugs for specific complaints

INDICATION	DRUG
Diarrhea or incontinence predominant	Loperamide (Imodium), 1-2 tablets, three times daily Antidiarrheal agent tightens anal sphincter Cholestyramine binds bile salts
Constipation predominant	Bran, 1 tablespoon three times daily and adjust Psyllium, 1 tablespoon three times daily and adjust
Gas, bloating, or flatus	Simethicone tablets, surfactant breaks up bubbles β-D-Galactosidase (Beano), with meals
Pain predominant	
Pain after meals	Dicyclomine (eg, Bentylol), 10-20 mg before meals
 Chronic pain 	Amitriptyline (eg, Elavil); individualize dose

Adapted from Drossman and Thompson. 28,29

Follow up. Follow-up visits are important to ensure the patient's conviction of the diagnosis, comprehension of its implications, and compliance with instructions. Those who have improved can be discharged, but should be warned that the symptoms might return periodically. The unhappy patient requires more attention.

Critique of drug therapy. After reviewing the published drug therapy trials, Klein concluded that "... not a single agent provides conclusive evidence that any therapeutic agent is effective in the global treatment of the IBS." ⁴⁹ In the United States, manufacturers are required to label products marketed for treatment

of IBS as "unproven." The sheer number and variety of drugs sold in Canada for IBS treatment are testimony to their collective uselessness. It seems unlikely that, with the variable symptoms of this syndrome and the complexity of the enteric nervous system, any drug aimed at specific function will make it all right. Advertisements that claim to relieve bowel spasm neglect to point out that bowel spasm cannot explain all of the clinical manifestations of IBS. Those that "regulate bowel function" are unclear about how this is achieved. All such agents lack a testable hypothesis.

The IBS is a chronic condition affecting many people, and any agent can evoke a 2- to 3-month placebo response. As physicians, we must consider the virtue of drugging large numbers of people with an agent of unproven efficacy when it is likely that young patients, convinced by the early placebo effect, will take the drug for long periods. The cost of such a policy would be very large, its efficacy doubtful, and the long-term risks uncertain.

Useful treatments. Despite these draw-backs, there are certain circumstances in which a drug is useful (Table 3). Some patients with IBS are particularly troubled by diarrhea, sometimes accompanied by socially embarrassing incontinence. Such patients can be helped by the timely administration of loperamide. One or two tablets can be given as needed, or before a social engagement, if one is careful not to precipitate constipation.

Sometimes pain is the dominant complaint. Rarely, the pain appears predictably after meals; perhaps it is an exaggeration of the cholinergically mediated gastrocolic response. ²³ In this case, an anticholinergic, such as dicyclomine, given before meals, interrupts this response, with minimal side effects. Sometimes the pain assumes some of the features and disability of the chronic pain syndrome. In that case, amitriptyline can have a salutary effect, even if depression is not obvious.

Predominant constipation is best treated by a bulking agent as discussed above. If bran fails, psyllium is a reasonable substitute. Those complaining of gas and bloating pose difficult problems. Bloating

is not due to increased intestinal gas. Occasionally, when gut transit is improved by bran, the bloating will also improve. For those complaining of excessive flatus who are unimproved by avoiding the "gassy vegetables," Beano can be tried. Beano, developed by a concerned bean industry, is a β -D-galactosidase, which, analogous to Lactaid, assists in the small intestinal digestion of certain carbohydrates before they can be attacked by gas-forming organisms. Available in supermarkets, this enzyme enjoys many anecdotal endorsements.

Psychologic and psychiatric disorders must be treated in their own right. Psychoactive drugs have little direct effect on IBS. One should avoid the benzodiazepines, because habituation is a risk in a chronic condition, such as IBS. More important is an empathetic discussion of the psychosocial state of the patient and some advice on exercise and stress management.

Referral strategy

The IBS is a chronic, recurring disorder. It is important that family doctors provide continuing care and especially avoid counterproductive overinvestigation. There are times, however, when referral becomes necessary. This can be rewarding if there is a specific problem to be addressed by a specialist and if, through good communication, the primary physician provides continuity of care.

Specific problems include pelvic pain in women, where a gynecologic examination is advisable. Sometimes the symptoms of IBS coincide with menses and endometriosis becomes a possibility. More often, however, IBS patients with pelvic pain are inappropriately labeled as having a gynecologic problem. 50-52 Suspected psychoses or severe depression are best handled by a psychiatrist. When the patient remains insecure of the diagnosis of IBS, referral to a gastroenterologist or internist can help. Authoritative confirmation of the diagnosis and validation of the management can make the primary physician's task easier.

Many exotic treatments are proposed. As can be imagined, these are difficult to evaluate, through double-blind trials, in a condition with such a notorious placebo

response to any treatment. It is, therefore, difficult to distinguish between quack remedies and those with a rationale and some serious attempt at validation. Generally speaking, those treatments based on diets, antiallergic drugs, or antiinfectious agents either have been discredited or lack any attempt at a scientific approach. Referral to advocates of such treatments is seldom helpful over the long term. However, respected researchers claim some success with such techniques as biofeedback⁵³ and hypnosis.⁵⁴ If practitioners of such therapies are available, they are harmless, and patients will at least benefit from the close attention.

For patients with excessive stress or social difficulties, a psychologist or stress management program can help.⁵⁵ Rarely the services of a pain clinic are required. The success of these referrals depends greatly on the continuing care and attention of the family doctor, to whom the specialist is a resource. Despite claims to the contrary, cure of the somatic symptoms remains the exception, and improved social and work functioning should be the goal.

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amoxicillin-clavulanate potassium

Antihiotic and R-lactamase inhibitor

INDICATIONS: Infections caused by susceptible &-lactamase-producing INDICATIONS: Infections caused by susceptible &-lactamase-producing strains of designated bacteria: upper respiratory tract and skin and soft tissue infections due to S. aureus, lower respiratory tract infections due to H. influenzae, K. pneumoniae, S. aureus or Moraxella (Branhamella) catarnhais; oritis media due to H. influenzae or Moraxella (Branhamella) catarnhais; urinary tract infections due to E. coli, P. mirabilis or Klebsiella species and sinusitis due to H. influenzae or Moraxella (Branhamella) catarnhais: CONTRALINDICATIONS: History of hypersensitivity to the penicillins, clavams or cephalosporins; infectious mononucleosis suspected or confirmed. WARNINGS: Before initiating therapy, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, clavams, cephalosporins or other allergens, as serious and occasionally fatal hypersensitivity lanachylactioid reactions have been reportsionally fatal hypersensitivity (anaphylactoid) reactions have been report ed. If an allergic reaction occurs, discontinue Clavulin and initiate approed. If all allergic reaction recently, inscending characteristic members appropriate therapy. Serious anaphylactoid reactions require immediate emergency treatment with epinephrine. Oxygen, i.v. steroids and airway management, including intubation, should also be used as indicated. PRE-CAUTIONS: Periodic assessment of renal, hepatic and hematopoietic CAUTIONS: Periodic assessment of renal, hepatic and hematopoietic function should be made during prolonged therapy. Clawlin is excreted mostly by the kidney. Reduce the dose or extend the dose interval for patients with renal dysfunction in proportion to the degree of loss of renal function. The possibility of superinfection (usually involving Aerobacter, Pseudomonas or Candidal should be kept in mind. If it occurs discontinue Clawlin and institute appropriate therapy. The progrupper of a morbilia-Pseudomonas or Candida) should be kept in mind. If it occurs discontinue Clavulin and institute appropriate therapy. The occurrence of a morbiliform rash following the use of ampicillin in patients with infectious mononucleosis is well documented. This reaction has also been reported following the use of amoxicillin. A similar reaction would be expected with Clavulin. Use in pregnancy is not recommended unless the anticipated benefit justifies the potential risk to the fetus. Penicillins have been shown to be excreted in human breast milk. It is not known whether clavulanic acid is excreted in breast milk. Caution should be exercised if administered to a nursing mother. ADVERSE REACTIONS: clavulanic acid is excreted in breast milk. Caution should be exercised if administered to a nursing mother. ADVERSE REACTIONS:
Gastrointestinal: Nausea, vomiting, diarrhea, abdominal cramps, flatulence, constipation, anorexia, colic pain, acid stomach and pseudomernbranous colitis. The incidence of gastrointestinal side effects tends to be proportional to dose and tends to be greater in children than in adults. Hypersensitivity Reactions: Erythematous maculopapular rash, urticaria, anaphylaxis and pruritus. A morbiliform rash in patients with mononucleosis. Rarely erythema multiforme and Stevens-Johnson syndrome have been reported. Liver: Transient hepatitis and cholestatic jaundice have been reported rarely. Moderate rises in SGOT, alkaline phosphatase and lactic dehydrogenase. The significance of these findings is unknown. Hemic and Lymphatic Systems. Anemia, thrombocytopenia, histophosphilia, leukopenia, lymphocytopenia, basophilia, topenic purpura, eosinophilia, leukopenia, lymphocytopenia, basophilia, slight increase in platelets, neutropenia and agranulocytosis have been reported during therapy with the penicillins. These reactions are usually reported during therapy with the penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. Other: Vaginitis, headache, bad taste, dizziness, malaise, glossitis, black hairy tongue and stomatitis. DOSAGE AND ADMINISTRATION: The absorption of Clavulin is unaffected by food. Adults: For urinary tract, upper respiratory tract, skin and soft tissue infections which are mild to moderate, one Clavulin-250 tablet every 8 hours. For severe infections and lower respiratory tract infections, one Clavulin-500F tablet every 8 hours. Children: For urinary tract, upper respiratory tract, skin and soft tissue infections which are mild to moderate, 25 mg/kg/day of Clavulin in equally divided doses every 8 hours. Children wighing more than 38 kg should be dosed according to the adult recommendations. For severe infections, otitis media, sinustits or lower respiratory tract infections, 50 mg/kg/day of Clavulin in equally divided doses every 8 hours. Children weighing more than 38 kg should be dosed according to the adult recommended for adults. Children weighing more than 38 kg should be dosed according to the adult recommended for adults. Children weighing more than 38 kg should be dosed according to the adult recommended for bad the commendations. For severe infections, streament should continue for 48-72 hours beyond the time the patient becomes asymptomatic or bacte-48-72 hours beyond the time the patient becomes asymptomatic or bacterial eradication is obtained. At least 10-days' treatment is recommended for infections caused by B-hemolytic streptococci to prevent acute

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