



## Post-infectious Irritable Bowel Syndrome: A Subtype of Irritable Bowel Syndrome

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### At a Glance

Bacteria are germs that can cause infection. Immune cells in the body fight infection. Inflammation is a sign that these cells are present. In some people, IBS begins after a bout of a bacterial illness in the GI tract, such as food poisoning. In those cases, certain immune cells continue to be present, even after the original illness is gone. These cells can cause pain and changes in stool.

- About 10% of people who suffer a bacterial GI infection develop “post-infectious” IBS.
- Certain things put some people more at risk for IBS after an illness including:
  - Age and psychological distress
  - Severity of the illness
  - Stressful life events in the months prior to the illness
- There is no treatment just for post-infectious IBS
- Current IBS treatments may be helpful
- Over time, about one-half of patients with post-infectious IBS will get better without treatment

Irritable bowel syndrome is one of the most common gastrointestinal (GI) disorders. It accounts for about 3% of all visits with primary care physicians. Within this large group of people, there is a small subgroup whose symptoms begin suddenly. It happens after what appears to be a bout of infection in the GI tract (gastroenteritis). This condition, first recognized during World War II, occurred in service men returning to the United Kingdom (UK) who had suffered from the illness amoebic dysentery. The symptoms in some persisted in spite of apparent cure of the infection. Later, in 1962, Chaudhary & Truelove described post-dysenteric irritable bowel syndrome in people who had suffered bacterial infections with *Salmonella* and *Shigella*. More recently, it has been described following a range of bacterial infections including *Campylobacter*, *Shigella*, and *Salmonella* species. The condition has been described in the UK, Korea, China, Spain, and Canada. After a GI infection caused by a virus post-infectious IBS seems uncommon, although brief bowel disturbances have been noted.

### How common is Post-Infectious IBS?

Considering all cases of IBS, between 6–17% of individuals with a previously normal bowel habit believe their illness began suddenly in association with an infectious illness. How often do persons who suffer bacterial gastroenteritis develop IBS? Depending on the study, the risk varies from 4–35%. Larger studies give a figure around 10%. Our own study of 747 individuals with stool cultures positive for *Campylobacter jejuni* is the largest in the current literature. We reported that at 6 months 103 (13.8%) had developed post-infective IBS. These cases were of the diarrhea predominant subtype of IBS in 63%, mixed subtype (alternating between diarrhea and constipation) in 24%, and constipation predominant subtype in 13%.

### Who gets Post-Infectious IBS?

Risk factors for post-infection include 1) the severity of the initial illness; 2) features in the infected person (host) such as age, gender, and psychological factors; and 3) the capability of the bacteria to produce a toxin. The strongest risk factors relate to the severity of the initial illness as measured by the length of time the acute diarrhea lasted. The host risk factors throw some light on likely mechanisms. Several studies indicate that psychological factors and adverse life events in the 3 months prior to infection increase the risk about two-fold. Females are more vulnerable to these factors and events, although gender does not appear to affect the immune system within the gut and its response to infection. No gender effect remains after controlling for psychological factors.

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Bacterial infections are usually spread by consuming contaminated food or water, or by contact with infected people or animals.

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Studies of the bacteria *Campylobacter jejuni* found that it produces a toxin that when present is more likely to produce persistent disturbance in bowel function. Interestingly, those over the age of 60 years had about one-third the risk of those aged 19 to 29. Vomiting during the initial illness (one of the ways the body tries to rid itself of harmful germs) also reduced the risk of post-infective IBS by around 50%.

## What are the Features of Post-Infectious IBS?

In our survey of 357 individuals with cultures positive for bacterial GI infection, the most common new symptoms were recurrent abdominal pain, loose or watery stools, urgent need to have a bowel movement, bloating, and passage of mucus through the rectum. A bowel movement typically relieves the pain. There is quite a range of severity. A minority get symptoms every day, while most have symptoms on 1–2 days per week.

## What Causes Post-Infectious IBS?

Acute GI infection with *Campylobacter jejuni* is known to cause an initial increase in inflammatory cells in the lining of the bowel and an increase in the serotonin-containing (enterochromaffin, or EC) cells. These changes gradually decline over the next few months but in those who develop post-infective IBS symptoms this decline is impaired. Indeed some persons have the same changes when studied many years later. The initial inflammatory response is found in all individuals. The abnormality appears to be a delay in the later down regulation (turning off) of the inflammatory response. This depends on both genetic and environmental factors and we now know that one type of blood cell that fights infection, the T regulatory cells, may play an important role.

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Inflammation is one way the body reacts to unwanted germs. It is part of a complex immune response. The immune system needs to turn on and turn off at the right times to fight infection and not cause harm.

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Associated with the increase in inflammatory cells, we also found an increased release of serotonin (5HT) after a meal. However, the link to the increase in inflammatory cells may be indirect since others have found a similar increase in serotonin release in patients with IBS and diarrhea, but who do not report a history of previous infection. Further research is needed to understand this link. Increased serotonin may well be important. Serotonin infusions induce nausea, vomiting and diarrhea. Drugs that block the action of serotonin (antagonists) are known to ease the symptoms of diarrhea predominant IBS, particularly the symptoms of urgency and loose stools.

Other researchers have looked for evidence of long-lasting inflammation and found prolonged changes in the barrier properties (permeability) of the lining of the intestines. These properties are important to prevent harmful substances from passing through into the body. This is something we have also noticed. Evidence of chemical messengers (IL-1) involved with inflammatory activation has also been found.

Changes in nerves in the gut lining may also be important. A study by Wang found evidence of increased substance P containing nerve fibers in areas of the intestinal lining. [Substance P is a neuropeptide (molecules made in the nerves) that enhances pain awareness.] This was associated with an increased number of mast cells in the small intestine where it joins the large intestine. This may be important because mast cells secrete substances that act on nerves

within the gut and may stimulate abnormal sensation including pain.

## Are there any Treatments for Post-Infectious IBS?

We tried an anti-inflammatory agent, prednisolone, to treat post-infectious IBS. But no benefit was seen in our small study. We chose to use only a short 3-week treatment course. During this course, we were not able to change the number of EC cells though we did decrease the number of infection fighting white blood cells, lymphocytes, within the intestinal lining. It may be that this course of treatment was too short. However, the side effects make it unlikely that patients will want to take this treatment for a longer period. There have been no other randomized control trials in post-infectious IBS, but for the reasons mentioned above drugs that block the action of serotonin on targeted receptors in the gut (5HT<sub>3</sub> receptor antagonists) might well be effective. Alternative treatments include symptomatic treatment of urgency and loose stools with loperamide (e.g., Imodium), though often at the price of increased bloating.

Given the possibility of long-lasting low-grade inflammation, an anti-inflammatory agent has obvious appeal. Probiotics may well have such a mode of action and two trials suggest benefit. One linked the benefit to a decline in inflammatory cytokines, a type of protein involved with immune responses. Probiotics have an excellent safety record but their effectiveness is uncertain. Moreover, different probiotics have completely different effects so no generalization is possible. We must evaluate each one on its own merits. So far, the studies seem to show very small effects. This suggests that either they are not effective or that we are failing to adequately characterize and target the patients who might benefit. Another possible anti-inflammatory treatment is the drug mesalamine (e.g., Asacol, Pentasa). Here again, no randomized trial has been done and the evidence so far is anecdotal.

## What is the Prospect for Recovery in Post-Infectious IBS?

Studies indicate that about one-half of patients with post-infectious IBS will recover with no specific treatment though this may take some years. The coexistence of anxiety or depression may reduce chances for recovery, though the numbers in our own study were very small and hence this finding should be viewed with caution.

## Further Reading

Spiller RC. Post-infectious irritable bowel syndrome. *Gastroenterology* 2003;124:1662-71.

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