Irritable bowel syndrome (IBS) is a common reason for younger persons to seek primary care. IBS patients are often unsatisfied when testing shows nothing is wrong and they feel that their concerns have been dismissed. Clinicians are often unhappy because they feel they have little help to offer and are reluctant to delve into psychosocial issues that are typically handled by a trained therapist.

Although IBS is a syndrome that may have multiple etiologies, excessive activity of brain and peripheral stress pathways plays an important role in many cases (2,4). High stress levels interfere with normal digestion, leading to decreased small intestinal and colonic transit times and increased fluid secretion. High levels of brain stress hormones (CRF) also appear to increase the brain’s sensitivity to pain (7). Visceral hypersensitivity can explain not only bloating and abdominal pain in IBS, but also the correlation of IBS with other poorly understood pain syndromes such as fibromyalgia.

IBS symptoms tend to correlate with current stress levels and may disappear entirely during a relaxing vacation. Patients who appreciate this link are more motivated to engage in stress reduction activities such as regular exercise, yoga, social activities and mindfulness meditation. They are also less likely to worry about having a severe undiagnosed illness.

Patients with a history of childhood sexual abuse are >4 times more likely to have unexplained somatic complaints (including IBS) (3).

More generally, Adverse Childhood Events (ACE) such as abuse or neglect have been shown to predispose very strongly to many common medical diseases including smoking, IVDA, HIV, alcoholism liver disease, risky sexual activity, CAD, depression, and suicide.(6).

Both human and animal studies have shown that ACE events can cause permanent epigenetic modification of the DNA coding for the brain glucocorticoid receptor, resulting in reduced receptor levels. This blocks inhibition of brain CRF expression by cortisol. High brain CRF is associated with anxiety, depression, insomnia, hypervigilance and visceral hypersensitivity (2,4).

IBS treatment can be very effective in many but not all cases:

IBS symptoms such as diarrhea, constipation and bloating should be treated with appropriate dietary and drug interventions. Probiotics, non-absorbable antibiotics, and low-dose tricyclics may help in selected cases. Antispasmodics work no better than placebo, but are safe and may significantly help some patients.

When the ACE score is elevated (3-4 or higher), addressing psychosocial factors can be helpful, including appropriate use of stress reduction, antidepressants and psychotherapy. The best results are achieved when the patient understands the role of stress in her disease and knows how to effectively deal with symptom flares.
Further reading


   This paper confirms earlier studies showing that physical and sexual abuse increase the risk of developing IBS and extends this finding to other forms of abuse (e.g., psychological) and neglect.

   Compared 284 adult IBS patients vs 435 healthy controls using a validated self-report form that covers physical, emotional, and sexual abuse as well as loss of a caregiver to death, incarceration or mental illness. All forms of abuse increased the risk of functional disorders, with psychological abuse a particularly strong predictor. IBS patients were more likely to answer yes to the following questions:

<table>
<thead>
<tr>
<th>Question</th>
<th>Odds Ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did you ever witness violence towards others, including family members?</td>
<td>2.08</td>
</tr>
<tr>
<td>Did anyone in your family ever suffer from mental or psychiatric illness or have a “breakdown”?</td>
<td>2.27</td>
</tr>
<tr>
<td>Were you often put down or ridiculed?</td>
<td>2.26</td>
</tr>
<tr>
<td>Were you often ignored or made to feel that you didn't count?</td>
<td>3.08</td>
</tr>
<tr>
<td>Were you usually treated in a cold, uncaring way or made to feel like you were not loved?</td>
<td>2.64</td>
</tr>
<tr>
<td>Were you ever forced or coerced to touch another person in an intimate or private part of their body?</td>
<td>2.92</td>
</tr>
<tr>
<td>Did anyone ever have genital sex with you against your will?</td>
<td>4.05</td>
</tr>
</tbody>
</table>

   *all p < 0.001


   Measured glucocorticoid receptor density in monocytes to test its postulated role in IBS. IBS patients had lower levels of glucocorticoid receptor mRNA that correlated inversely with symptom severity. Severe symptoms also correlated with a history of early adverse life events (ACE). These findings are consistent with the hypothesis that severe IBS patients have an abnormally reactive stress response due to decreased negative feedback via the glucocorticoid receptor. Measurement of glucocorticoid receptor expression in peripheral blood cells can be used to assess the activity of human stress pathways.

3. Park SH, Videlock EJ, Shih W, Presson AP, Mayer EA, Chang L, **Adverse childhood experiences are associated with irritable bowel syndrome and gastrointestinal symptom severity.** *Neurogastro Motil (in press)* 2016 (PMID:27061107)

   An elevated ACE score was strongly associated with IBS severity in 148 IBS patients vs 154 controls. Emotional abuse and household history of mental illness were particularly strong predictors.

*First human example of “imprinting” by ACE events. Suicide victims with an ACE history had much higher levels of epigenetic inactivation of the glucocorticoid receptor in the brain compared to suicide victims with no ACE history. Inactivating this receptor causes high levels of CRF in the brain, which predisposes to anxiety, depression and multiple somatic complaints.*

![Graph](image)

**Figure 1.** Childhood abuse reduces expression of brain glucocorticoid receptor mRNA by > 50% in humans. Suicides victims were studied because access to brain tissue was required.

5. Dias BG, Ressler KJ. **Mice Inherit the Fears of their Fathers:** Nat Neuroscience **17:**89-96 2016 [http://www.nature.com/news/fearful-memories-haunt-mouse-descendants-1.14272](http://www.nature.com/news/fearful-memories-haunt-mouse-descendants-1.14272)

*Animal study shows that stress experienced by parents affects their offspring. Male mice were trained to associate a certain smell with electric shock. First and second generation offspring of these mice displayed a “startle response” when exposed to the same smell, but not other smells. This held true even when the offspring were fertilized by artificial insemination. Concludes that learned responses to danger can be inherited epigenetically.*

6. **Adverse Childhood Experiences (ACE) study.** Centers for disease Control (ongoing) [http://www.cdc.gov/ace/findings.htm](http://www.cdc.gov/ace/findings.htm)

*Ace score of 4 or more roughly triples the risk of many common medical diseases including anxiety, depression, alcoholism, COPD, ischemic heart disease, IVDA, liver disease, STDs, having >50 sexual partners and risk of perpetrating domestic violence.*

7. Camilleri M, Coulie B, Tack JF. **Visceral hypersensitivity: facts, speculations, and challenges.** Gut 2001 **48:**125M131. [http://gut.bmj.com/content/48/1/125.full](http://gut.bmj.com/content/48/1/125.full)

*Review of visceral hypersensitivity, which appears responsible for most pain in IBS*