Inflammation of the gastrointestinal tract is common in Ankylosing Spondylitis (AS). Up to 60% of AS patients who have no gastrointestinal symptoms will have microscopic (on biopsy) inflammation in the gut when colonoscopy is performed. Most of these patients do not develop overt inflammatory bowel disease (IBD) like Crohn’s disease or Ulcerative colitis. Recent studies show about 3-4% of patients have IBD when they are diagnosed with Ankylosing Spondylitis, but after 20 years, approximately 10% have IBD.

Patients with Ankylosing Spondylitis and IBD share similar important genetics. The gut and joint inflammation on a shared genetic background highlights the importance of this connection and how these are related diseases. Data shows that patients with AS have first degree relatives with a 3-fold higher risk of Crohn’s disease, and patients with Crohn’s disease have first degree relatives with a 3-fold higher risk of Ankylosing Spondylitis.

Just as patients with AS can develop IBD, patients with Crohn’s disease and Ulcerative colitis can also develop arthritis. This can occur in the sacroiliac joints and spine (and is identical to Ankylosing Spondylitis) and/or in the smaller joints of the extremities (knee, ankle, feet, hands etc). The most common joint manifestation is the sacroiliac joint - affecting 10-20% of patients with IBD. Note that some of these patients will not have SI joint pain, and the finding is often noted on imaging done for other reasons (like a CT scan done for IBD). The sacroiliitis (back/buttock and hip involvement) can occur when the IBD is silent or active and can continue even when patients undergo colectomy in Ulcerative colitis.

The small joint arthritis can behave differently. There are two types of small joint arthritis (along with the arthritis in the SI joint) described in Table 1 below.

### Table 1. Arthritis types in IBD

<table>
<thead>
<tr>
<th></th>
<th>Type I Arthritis</th>
<th>Type II Arthritis</th>
<th>Spondylitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>What percent of IBD patients are affected?</td>
<td>3-6%</td>
<td>2-4%</td>
<td>~ 20%</td>
</tr>
<tr>
<td>What joints are usually affected?</td>
<td>Large joints in legs - knee, ankle, foot</td>
<td>small joints in hands - wrist, fingers</td>
<td>Sacroiliac &amp; spine</td>
</tr>
<tr>
<td>How many joints are typically affected at 1 time</td>
<td>&lt; 5</td>
<td>&gt; 5</td>
<td>n/a</td>
</tr>
<tr>
<td>Can occur when?</td>
<td>At first sign of IBD</td>
<td>After the onset of IBD</td>
<td>Often in younger patients</td>
</tr>
<tr>
<td>Disease course</td>
<td>Acute &amp; remitting</td>
<td>Chronic &amp; relapsing</td>
<td>Typically chronic</td>
</tr>
<tr>
<td>With IBD activity</td>
<td>Yes</td>
<td>Not necessarily</td>
<td>Not necessarily</td>
</tr>
</tbody>
</table>

### Medications for Arthritis associated with IBD:

The treatment of the joint disease in IBD depends on which joints are affected and whether the IBD is also active.

If the sacroiliac joints are affected, then the appropriate treatment is either a drug class called Non-steroidal anti-inflammatory drugs (NSAIDs) which are sometimes contraindicated in patients with IBD because of the concern for IBD flares in the setting of these agents, or the biologic agents. Examples of NSAIDs are ibuprofen or naproxen over the counter; celecoxib is sometimes preferred as it may be safer in the gastrointestinal system, though the evidence of this in IBD is weak. The American College of Rheumatology recently published guidelines in Axial Spondyloarthritis and did not recommend a preferred NSAID in the setting of IBD because of the weak evidence. If NSAIDs are not a possibility, then the only other class of drugs with proven efficacy at this time is the biologic agents - Tumor Necrosis Factor Inhibitors (TNFI). For patients with sacroiliitis and IBD, a certain type of TNFI is preferred, called a monoclonal antibody. See table 2 for specific drugs.

In the setting of small/peripheral joint arthritis (the arthritis affecting the joints of the extremities) the treatment depends on whether the IBD is active. If there is IBD activity, then the recommendation would be to treat the underlying IBD. If the IBD is quiet, then we would use the usual agents for small joint arthritis including sulfasalazine, methotrexate, azathioprine, and/or low doses of prednisone temporarily, or the biologic agents, like the TNFI. Besides the NSAIDs, all the medications listed below in table 2 may also help the IBD.
Another TNFI, Etanercept (Enbrel) works for the joints, but not the IBD and is generally not preferred if there is IBD in the presence of the arthritis. In this group, the TNFI listed in table 2 are preferred.

For those patients with IBD that is resistant to TNFI, their gastroenterologists might consider a new drug, Vedolizumab. This drug works by staying inside the gut, but as a result will not treat the arthritis, if this is occurring independent of the GI disease activity.

Besides arthritis with inflammation, patients with IBD can have other reasons for joint pain and arthritis. IBD patients can be more hypermobile (very flexible) which may lead to joint injury and pain. Patients with or without IBD can develop osteoarthritis – arthritis as a result of wear and tear. Though this can happen from the arthritis associated with the IBD after long bouts of inflammation, these are more commonly not thought to be inflammatory and are treated conservatively with pain control and physical therapy. Occasionally, the arthritis is severe enough to require joint replacement – especially in the hips and knees. This procedure can dramatically improve quality of life in patients who have joints with severe damage. Finally, patients with chronic disease may also develop a widespread pain syndrome called Fibromyalgia, which is not immune mediated or associated with inflammation, but can be very disabling and is treated with regular exercise, cognitive behavioral therapy and occasionally pharmacologic therapy.

References:
These recommendations are intended to provide doctors, physical therapists, and other clinicians who care for patients with AS and related types of spondyloarthritis with guidance on approaches to treatment that are based on current and best-available medical research. Given the wide diversity of medical conditions and the breadth of medical knowledge, it is sometimes difficult even for subspecialists, such as rheumatologists, to be fully up-to-date on the treatment options and alternatives to consider in all types of situations.

In developing these recommendations, we posed questions on the most common and important treatment considerations facing patients with AS and their doctors, and attempted to answer them through a comprehensive review and summary of the medical literature on each topic. For questions that had not been studied well or at all, we relied on the judgment of a group of physicians and therapists who had a great deal of experience in treating patients with AS. We also considered the strength of the evidence for or against the treatment alternatives posed by each question, and the degree to which patients might deliberate and differ over the decision to use one treatment versus another, in considering the weight to give each recommendation.

There are three important points that patients should keep in mind regarding these recommendations. First, these are not a set of rules that doctors must follow. There are many reasons why a particular recommendation may not be followed for an individual patient, including their prior medical history, other co-existing illnesses or medications, their stage of AS, and considerations of the trade-offs between the potential benefits and harms of a given treatment choice. Think of these more as a resource guide that doctors can use to help their decision-making in recommending (or not recommending) particular tests or treatments. All treatment decisions must be individualized to fit the patient and his or her particular circumstances.

Second, the recommendations don’t consider all possible issues or questions that can occur in patients with AS or spondyloarthritis. The recommendations focused on the most common questions, but many others remain. We hope that these recommendations can be expanded to include more questions in the future.

Third, these recommendations are not unchangeable. While they are based on the best evidence available to date, new research may uncover new findings that would cause us to change a recommendation. This would be unlikely for recommendations that were designated as a “strong” recommendation, because the evidence for these was considered so solid that any new research was thought very unlikely to change the conclusion. However, for “conditional” recommendations, new research may change the recommendation as more facts are learned. Also, new treatments may be developed that would change our thinking about the way patients should be treated in particular circumstances. Or new information about side effects of treatment may be produced to change our ideas about the safety of a given treatment. It is important to note that most of the recommendations were conditional ones. To make sure the recommendations stay up-to-date, we plan to review them every few years, and issue updates earlier if important breakthroughs occur that make a current recommendation obsolete.

Michael M. Ward, MD is Senior Investigator at the Intramural Research Program at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) at the National Institutes of Health (NIH). Please note that the guidelines are not produced or endorsed by the NIH.