Ulcerative Colitis: Symptoms and Treatments

Patient: ___________________  _/__/20__

<table>
<thead>
<tr>
<th>[Name of Disease]</th>
<th>Ulcerative Colitis</th>
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<tbody>
<tr>
<td><strong>Type of Ulcerative Colitis</strong></td>
<td>Ulcerative Proctitis</td>
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<td><strong>Activity Pattern</strong></td>
<td>First flare-up</td>
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<td><strong>Current State of Disease</strong></td>
<td>Active</td>
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<td><strong>Severity Level</strong> (Based on Japanese Ministry of Health and Welfare standards)</td>
<td>Light</td>
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[What is Ulcerative Colitis?]

Ulcerative Colitis is a chronic disease in which inflammation and ulcers develop repeatedly in the mucous membranes of the large intestine. Although the root cause of the disease is currently unknown, it is believed that attacks of the disease are the result of an abnormality in the immune system. Once inflammation occurs, the most common symptoms include: Diarrhea, abdominal pain, and stools in which mucous is present. Moderate to severe symptoms include: Fever, bloody stools, bloody diarrhea, and anemia.
Currently recognized types of Ulcerative Colitis and affected areas in the colon

- Light
- Moderate
- Severe

Light inflammation on surface of mucous membranes
Inflammation and moderate ulceration
Heavy inflammation leading to swelling and severe ulceration

Type of exam used to diagnose Ulcerative Colitis:

| Barium X-Ray | Full Colonoscopy | Abdominal CT scan | Ultrasound |

Severe Inflammation / Intractable Case?

| Yes | No |

Severe Inflammation
The result is deep ulceration due to severe inflammation and intense swelling (edema) in the mucous membranes of the large intestine. Visible symptoms include abdominal pain, fever, and bloody stool / bloody diarrhea. Risk of deterioration of nutritional health and secondary infection to the patient require that appropriate treatment be received immediately. During the course of internal medicinal treatment, a sudden onset of severe bleeding or a general decline in condition due to a secondary infection can cause perforation of the colon (a hole opens in the wall of the large intestine), toxic mega-colon (the nerves in and around the large intestine become paralyzed),
and other serious complications. For patients with these complications and patients who do not respond well to internal medicine, the possibility of surgical treatment must be taken into account.

◎ **Intractable Case**
Despite receiving proper internal treatment patients who experience frequent flare ups of chronic inflammation, steroid dependency, or who don't respond to steroid treatment may unfortunately have an intractable (incurable) cases. For patients in this condition it is necessary to investigate whether some cause of the increased disease activity can be determined (for example a secondary infection) and to obtain up-to-date information on the condition of the colon in order to determine which steps to take in treatment.

[Treatments for Ulcerative Colitis available at our IBD Center]

◎ **Remission Period**

¬ 5-aminosalicylic acid (5-ASA) based medications such as Pentasa®, Salazopyrin®, and Asacol® are generally administered as maintenance drugs in order to prevent flare ups of Ulcerative Colitis. In addition to helping prevent relapses of the disease and hinder the spread of inflammation, this medicine plays a major role in treatment as it has proven effective in controlling light to medium cases of inflammation and reduces the long term risk of colon cancer.

¬ Pentasa® and Asacol® are commonly used 5-ASA drugs, referred to generically as mesalamine. Both have few side effects, and both contain few ingredients which dissolve in water (localizing the release of medicine to the colon). Salazopyrin® is a drug derived from the same ingredients as Pentasa® but it contains an extra ingredient sulfapiridine that helps suppress inflammation. This compound exhibits an even stronger anti-inflammatory result than Pentasa®. However, the major concerns with Salazopyrin are that a slightly high percentage of patients allergic to the sulfapiridine, and sperm count in males can drop temporarily.

¬ For patients who continue to experience flare ups despite receiving 5-ASA treatment, immuno-suppressants Imuran® and Leukerin® are recommended for temporary periods of
time. Although these drugs take several months to achieve efficacy, they are known to work well on Ulcerative Colitis.

During periods of remission, many patients can live relatively normal lives with few dietary restrictions. As excessive and chronic stress can lead to a relapse of Ulcerative Colitis, it is important to maintain good sleep habits, attempt to minimize stress and lead a lifestyle that maintains a normal routine. In general, patients with Ulcerative Colitis in remission can exercise, go to school, maintain a career, and in the case of women, bear children normally. Any restrictions to the patient’s lifestyle depend on the patient’s health and the medication(s) he or she is taking, so be sure to check with your gastroenterologist if you are unsure about a certain aspect of your lifestyle.

Active Period
The damage suffered by the large intestine during periods of inflammation is comparable to tissue of the human body which has suffered a burn. Long-term inflammation can make it even more difficult for a patient to enter remission. In cases of severe inflammation, patients are often hospitalized, must abstain from all foods, and are given intravenous medication. The goal is to let the large intestine rest and to enter remission. During this critical time one or more of the following treatment methods is administered.

Corticosteroids (Predonine®)
Corticosteroids (henceforth “steroids”) are administered with the purpose of suppressing the immune system and inflammation causing adrenal hormones that are made naturally within the body. This treatment reliably controls inflammation caused by Ulcerative Colitis and has a high rate of success in patients. However, since it is a hormonal treatment it comes with a host of side effects and cannot be long term without risk. As such, the dosages and period of use must be carefully managed by your gastroenterologist.

Leukocytapheresis (GCAP, LCAP)
The GCAP and LCAP treatments remove agitated and overactive white blood cells (one cause of inflammation) from inside the bloodstream in a blood filtering treatment process similar to dialysis. The treatments have few side effects and are safe, however the success rate is around 60% and severe cases of Ulcerative Colitis show only slight improvement. Since these treatments take time to show results, steroids are often administered simultaneously.

**Immuno-suppressants (Cyclosporine®, Neoral®)**
These medications are powerful immuno-suppressants administered intravenously. Through a totally different mechanism than steroids, immuno-suppressants have a 70% success rate for patients who have severe inflammation or who are unresponsive to steroids. The treatment requires that patients receive medication intravenously 24 hours a day for two weeks. Due to the heightened risk of secondary infections and the many side effects of immuno-suppressants, hospitalization and strict management of the patient's bodily health and immune system must be undertaken alongside this treatment.

**Immuno-suppressants (Tacrolimus®)**
Using the same mechanism as Cyclosporine®, Tacrolimus® can be taken orally and is an effective treatment for Ulcerative Colitis. In clinical studies, 50% of patients with severe symptoms responded well to Tacrolimus®, and 70% with light to moderate symptoms saw improvement of their conditions using this powerful treatment. Typical administration of the drug involves a high dose for two weeks followed by a three-month treatment period at a lower dose. Special precautions must be taken with this medicine as it compromises the patient's immune system, however Tacrolimus® has few other side effects and shows promise as a new and effective treatment for patients who do not respond well to steroids.

**TNFα inhibitor Infliximab (Remicade®)**
Heralded as a break through drug for Crohn's disease, this biological therapy quickly and powerfully suppresses outbreaks of inflammation. First approved for use in Japan
for Crohn's patients in 2002 and later for Ulcerative Colitis patients in 2010, Infliximab is currently administered to more than 800,000 patients with Rheumatism, Psoriasis, Crohn's Disease, and other inflammatory diseases worldwide. Treatment is administered intravenously, and typically maintains efficacy for eight weeks. Success rates are lower for Ulcerative Colitis patients, in the 50% range, however for those patients who respond well to Infliximab the treatment has a quick-acting effect not seen in other Ulcerative Colitis drugs. Hospitalization is required for the first treatment, however subsequent treatments can be performed as outpatient procedures (one round of intravenous treatment takes about 3 hours).

Side Effects: Risk of infection, worsening of stricture symptoms, allergic reactions to Remicade, and abnormal immune system reactions. As Infliximab is a relatively new medicine, long term side effects (elevated risk of cancer, for instance) are still unknown, however at this point it is accepted that even pregnant women have been able to use Infliximab safely. Using Infliximab long term has been known to gradually result in a resistance to it, which can become problematic.

**Antibiotic treatment for secondary intestinal infections**

Secondary infections can result from an intestinal bacteria imbalance, or a virus lying dormant in the patient's body that suddenly becomes active. Should such a complication occur, antibiotics have proven an effective in treating intestinal infections.

© **Surgical Treatments (Colectomy)**

If, despite receiving appropriate treatment, the patient's condition does not improve and remission cannot be achieved, surgical removal of the large intestine (colectomy) may be unavoidable. Generally, surgical treatment is recommended for the following cases:

1. Due to massive intestinal bleeding, the patient's life is at risk.
2. Despite continuing maintenance treatment, the condition of the patient does not improve and the case appears intractable.

3. Patient suffers (or has a high risk of suffering) severe medicinal side effects and continuing treatment is undesirable.

4. Patient experiences multiple relapses of the disease and hospitalizations, or patient becomes dependent on steroids to maintain remission.

5. Cancer or precancerous lesions are found in the large intestine or the patient's risk of cancer is considered high.

For patients whose conditions have worsened in the above manners, the affected area (namely the large intestine) is entirely removed and the patient typically experiences a vast improvement in his or her condition. On the other hand, surgery and anesthesia carry risks of complication, and patients must also be aware that intestinal obstructions and incontinence can occur in some cases after surgery. Therefore it is recommended that patients consult a specialist in colorectal surgery to determine whether surgery is the appropriate step to take in treatment.

[Other treatments: Treating complications]

When a patient is hospitalized in our Inflammatory Bowel Disease (IBD) center, our staff of gastroenterologists, colorectal surgeons, nurses, pharmacists, and dietitians are constantly discussing which treatment is appropriate for each individual. Our staff comprehensively considers each patient's case; including overall condition, disease history, medications and dosages, susceptibility to side effects, lab / test results etc., then a consensus is made on how to properly adjust our treatment methods to each patient's needs. For any questions or concerns, be sure to consult your gastroenterologist.
(For detailed explanations of all treatments and surgical procedures listed here, please refer to the other informational packet(s) enclosed within).

Consultant: Yokohama City University Medical Center, IBD Center

Doctor _____________________________________

Person(s) receiving consultation:

Patient _____________________________________

Family Member ______________________________

Relation ____________________________________

Translated by Spencer Bartz (Sept 1st, 2011)