

Crohn's Disease: Symptoms and Treatments

Patient: _____

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[Name of Disease]		Crohn's Disease (Regional Enteritis)	
Classification	Ileal (small intestine type)	Ileocoloic (small and large intestine type)	Colonic (large intestine)
Disease Activity			
Fistula	Not Present	Present (Location:)	
Activity in anal region	None	Fistula • Skin Tag • Inflammation • Ulceration • other	
Activity in upper digestive tract	None	Esophagus • Stomach • duodenum	
Current condition of disease	Remission	Active	
Other coexisting ailments:			

[What is Crohn's Disease?]

Crohn's Disease is an chronic Inflammatory Bowel Disease (IBD) that affects the entire digestive tract from the mouth to the anus. The nature of the disease causes recurring inflammation and ulceration in the mucous membranes of the intestines. It is believed that an abnormality in the immune system plays some role in the recurring nature of the disease. Common symptoms include (but are not limited to) diarrhea, bloody stool, fever, and weight loss. Should a continuous cycle of severe inflammation occur, stricture (narrowing of the intestines), fistula (an abnormal passage between two organs or vessels that normally do not connect), and other complications may occur, causing a high level of damage to the gastrointestinal tract.

[Current classification and extent of your case]

	Moderate	Inflammation and moderate ulceration
	Severe	Heavy inflammation leading to swelling and severe ulceration

Moderate Case: Inflammation / tissue erosion, shallow ulceration

Severe Case: Severe inflammation due to edema (intense swelling), deep ulceration

Type of exam used to diagnose Crohn's Disease:			
Barium X-Ray	Full Colonoscopy	Abdominal CT scan	Ultrasound

[Current Problematic Areas]

-Multiple areas of severe ulceration develop in the digestive tract resulting in chronic inflammation in deeper layers of the intestines. As a result, intense abdominal pain, diarrhea, fever, malnutrition, and weight loss appear as common symptoms.

-As Crohn's Disease affects the entire digestive tract, scarring (fibrosis) may

cause strictures (narrowing of the digestive tract) which lead to bowel obstructions.

-A fistula (an abnormal tube like connection between two parts of the intestine that don't normally connect) can form, leading to complications.

-Infections caused by deep ulceration can lead to the formation of abscesses (a cavity in the tissue filled with puss) and cause even more inflammation in the vicinity of the abscess.

[Our Fundamental Treatment Approach to treating Crohn's Disease]

In addition to using the standard anti-inflammatory drug Pentasa® the following treatment methods are utilized at the Inflammatory Bowel Disease (IBD) Center:

1. Treatment of Crohn's via dietary measures

- ⤴ Patients must completely abstain from food and receive nutrition intravenously through a catheter inserted into a central cardiac vein. This is often referred to as Intravenous Hyper-Alimentation (IVH) in Japan, and Total Parenteral Nutrition (TPN) in the USA. A dietary supplement called Elental® is also used to supply adequate nutrition.
- ⤴ By abstaining from food, the affected areas of the intestines are able to rest, and with proper dietary replenishment, healing of the ulcerated areas in the intestines is hastened. Additionally, antibody reactions to antigen-containing-food appear to be the root cause of Crohn's disease. This implies that some antigens cause the immune system to react abnormally and create proteins to attack the antigens as if they were a threat to the digestive tract. In order to avoid these abnormal reactions and relapses of the disease, the disease is managed in a gradual manner. In addition, maintaining a good balance of bacteria in the digestive tract, using Amino Acid medication heals damage in the digestive tract, and helps suppress inflammation. This form of treatment not only has nutritional benefits for patients of Crohn's Disease, it is also known to produce positive results when treating the disease itself.
- ⤴ Without the use of powerful medications and chemical compounds, this form of treatment is favored due to its safety and lack of side effects, however it is also the slowest to show improvement in the patient's condition. Patients are typically hospitalized for one month, and after discharge must continue

the treatment for several months.

- ✦ This type of dietary treatment works especially well in the small intestine, but exhibits less satisfactory results in treating severe inflammation in areas of the large intestine.

2. Adrenal Cortex Hormone Therapy (Corticosteroids, Predonine®)

-In severe cases of the disease, Corticosteroids (hereafter "steroids") are one of the most highly effective medications commonly used to treat inflammation. Steroids have long been used as a general method to treat auto-immune diseases. As a result, doctors have accumulated a lot of knowledge and experience in regard to the drug's efficacy, safety, and side-effects. Although it is a powerful type of medication, it has no known risk of causing cancer. In terms of Crohn's disease cases, it is known to be most effective in the large intestine.

-During periods of severe inflammation, hospitalization is necessary and steroid treatment is administered intravenously. Following discharge from the hospital, patients can take steroids orally under the supervision of a gastroenterologist. Initially a relatively high dose is used, then as the inflammation subsides, the dosage can be gradually tapered off. Once the patient's condition has entered a state of remission, steroid treatment can be discontinued. This process typically takes several months.

-Due to the nature of this type of hormone therapy, there are many side effects. The appearance of each side effect may vary with time, and it is rare for a patient to experience *all* side effects of steroid therapy. While administering steroids, blood test results and symptoms are carefully monitored as treatment continues. In the event that side-effects do occur, inform your your gastroenterologist and he or she will promptly decide how to appropriately deal with any complications.

Side Effects of Steroids:

- Increased risk of infections
- Osteoporosis
- Higher risk of broken bones and growth impairment (in children)
- Phlebosclerosis (Thickening of the walls of the veins)
- Adrenal Insufficiency
- Symptoms involving mental health (Steroid Psychosis)

- Insomnia
- Accelerated appetite (not feeling full despite eating normally)
- Peptic ulcers, gastritis
- Diabetes Mellitus
- High Blood Pressure
- Hyperlipidemia (elevated levels of lipids in blood)
- Cardiac Arrhythmia (abnormal heart-rate and cardiac rhythm)
- Heart Failure
- Cataracts
- Glaucoma
- Moon Face (weight gain localized to the facial area)
- Central Obesity (weight gain localized to the abdominal area)
- Pilois (abnormal and/or excessive hair growth)
- Subcutaneous Bleeding (hemorrhaging under the skin)
- Acne
- Stretch marks (from weight gain)
- Paridrosis (excessive perspiration)
- Hot flashes, burning sensations
- Exophthalmos (Projecting of the eyeball out of the socket. Also known as exophthalmia or proptosis)
- Edema (fluid accumulates beneath the skin, causing swelling)
- Myositis (inflammation of muscle tissue)
- Abnormalities in menstrual cycles in women
- Elevated white blood cell count

3. Immunosuppressants (Imuran®, Leukerin®)

-Can be taken orally, and both are commonly used in Europe and North America.

-While these medications are slow to achieve efficacy (taking possibly several months), they are especially effective in preventing relapses of Crohn's disease and have a 70% success rate.

Side effects include but are not limited to:

- Bone marrow suppression
- Low white blood cell count
- Risk of secondary infections
- Hair loss
- Hepatitis
- Pancreatitis
- Fever

-Patients who experience side effects are known to be predisposed to hereditary factors, however there is currently no way to identify such a predisposition before administering.

-Assuming the patient does not suffer the side-effects listed above, immunosuppressants can be administered more steadily than steroids.

-Normally, as these drugs alone will not fully suppress active inflammation in many patients, steroids or dietary treatment are used in combination with immunosuppressants. On average, the treatment process can take two months to one year to become fully effective.

-Often times the drug is administered for as long as two to five years. Once the disease activity has subsided, the patient may stop taking the medication.

4. TNF alpha inhibitor: Remicade® (Monoclonal Antibody infliximab)

-This treatment is currently the fastest and most effective in suppressing inflammation due to Crohn's disease. First approved for use in Japan in 2002, Infliximab (pharmaceutical name: Remicade®) is currently administered to more than 800,000 patients with Rheumatism, Psoriasis, Crohn's Disease, and other inflammatory diseases worldwide.

-A more powerful treatment than steroid therapy, Infliximab can suppress inflammation reliably, is administered intravenously and remains effective for up to eight weeks. With at least an 80% success rate in the short term for Crohn's patients, Infliximab works quickly and can greatly reduce the time a patient must be hospitalized.

-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 include but are not limited to:

- Increased risk of infections
- Worsening of stricture symptoms
- Allergic reactions to the drug itself
- Other abnormal immune system reactions

-As Infliximab has only been available in Japan since 2002, long term

side effects (increased risk of cancer, for instance) are still unknown, however at this point it is known 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. In Crohn's patients who have undergone Infliximab treatment, about 20% develop a resistance, however the drug is said to be effective in long term use for 50% to 60% of patients. Additionally, children are reported to develop a resistance to the drug more easily than adults. As the mechanism which causes this resistance is still unknown, clinical trials are underway to adjust the method of administering the drug, the dosage, and to combine other drugs to prevent resistance.

Humira® (Adalimumab)

-Using the same technique as Infliximab (TNF Alpha inhibitor) Humira is administered via hypodermic injection. Humira treatment does not require hospitalization, long periods of intravenous drip, or even an outpatient procedure. Patients may inject Humira in the comfort of their own homes, at a frequency of once every two weeks.

-While Humira is less effective in treating Crohn's disease than Infliximab (effective for 40 to 50% of patients), significantly less allergic reactions to the drug have been reported.

5. Leukocytapheresis (GCAP)

-The GCAP treatment removes agitated and overactive white blood cells (one cause of inflammation) from inside the bloodstream in a blood filtering treatment process similar to dialysis. Treatment sessions last about one hour and are carried out once a week. The typical treatment period can be anywhere from five to ten weeks. GCAP was originally used to treat Ulcerative Colitis, but in 2009 it was adapted to treat Crohn's Disease as well and is now covered under Japanese medical insurance.

-The treatments have few side effects and are safe, however the success rate is lower than Ulcerative Colitis, at about 40 to 50% for Crohn's Disease patients. Specifically GCAP is less effective in treating inflammation in the small intestine, severe inflammation in the large intestine, and has a low rate of success in suppressing disease activity in the anus. It may take several weeks before the patient shows any improvement, and the rate of relapse after stopping the treatment is relatively high. Finally, many patients of

Crohn's Disease have narrow veins which can make starting a GCAP session difficult or nearly impossible. One solution is to insert a central line catheter into an artery that leads directly to the patient's heart, making each procedure relatively easy and less painful.

6. Antibiotic treatment for secondary intestinal infections

-In the case of secondary infections or complications resulting from an imbalance in intestinal bacteria, use of antibiotics has been proven to be an effective form of treatment. Infections may also occur from deep ulceration or the development of an anal fistula, in which case antibiotics will also be prescribed.

The damage caused by Crohn's disease in the large intestine during periods of inflammation is comparable to tissue of the human body which has suffered a burn. If left untreated for long periods of time, it can become more difficult to attain remission using internal medicine. Additionally, if the inflammation progresses deep into the intestinal lining, or if the patient suffers continuous relapses, parts of the digestive tract may become narrower (due to scarring) and cause intestinal blockages. Emergency surgery is necessary to resolve such a blockage, so it is important to seek proper medical care before such a complication occurs.

The treatment methods listed above have been clinically tested and a thorough amount of data regarding the effectiveness and safety of each has been gathered and evaluated by the Japanese Ministry of Health, Labor, and Welfare. All of the treatments used at our IBD center are based on their guidelines.

7. Surgical Treatments

Despite receiving standard treatment, if the patient's condition does not improve and remission cannot be achieved, surgical removal of the diseased area is recommended. Generally, surgical treatment is recommended for the following cases:

- Due to severe intestinal bleeding, the patient's life is at risk.
- Despite continuing maintenance treatment, the condition of the patient does not improve, shows no signs of improvement, and a high risk of fibrous stenosis (narrowing of the intestine due to swelling and repeated inflammation and scarring) is assumed.
- An internal fistula (an abnormal passageway between two parts of the intestines) develops and causes bowel obstructions or

inflammation.

-An abscess develops in the abdominal region and the patient's condition does not improve despite the use of antibiotics or other internal medicine.

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

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

For patients whose conditions match the above cases, the affected area is surgically removed and the patient typically experiences an 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. Furthermore, as Crohn's disease is not entirely cured by surgical means, continuing preventative care in the form of internal medicine is necessary. Of course, before any surgical action is taken, it is recommended that patients consult one of our specialists in colorectal surgery to determine whether surgery is the appropriate step to take in treatment.

[Notes: Treatments for complications etc.]

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 that 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 _____