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**Ministry of Higher Education & Scientific Research 4th class (Lecture 11)**

**Al-Rasheed university College Clinical immunology**

**Department of medical laboratory 2021 / 2022 techniques**

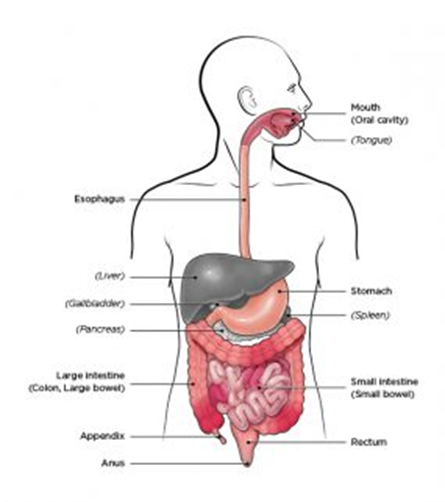
**Inflammatory bowel disease**

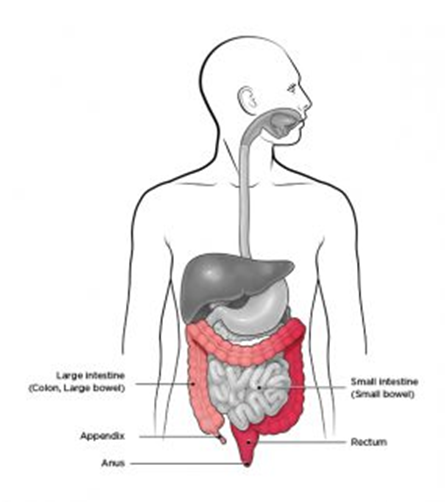
\*Inflammatory bowel disease (IBD) is a group of inflammatory conditions of the colon and small intestine. Crohn's disease and ulcerative colitis are the principal types of inflammatory bowel disease. It is important to note that not only does Crohn's disease affect the small intestine and large intestine, it can also affect the mouth, esophagus, stomach and the anus whereas ulcerative colitis primarily affects the colon and the rectum.

\*Some of the differences between Crohn’s disease and ulcerative colitis:

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| --- | --- |
| **Crohn’s Disease** | **Ulcerative Colitis** |
| Can affect any part of the GI tract (from the mouth to the anus)—Most often it affects the portion of the small intestine before the large intestine/colon. | Occurs in the large intestine (colon) and the rectum |
| Damaged areas appear in patches that are next to areas of healthy tissue | Damaged areas are continuous (not patchy) – usually starting at the rectum and spreading further into the colon |
| Inflammation may reach through the multiple layers of the walls of the GI tract | Inflammation is present only in the innermost layer of the lining of the colon |
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**1**

**Crohn’s Disease **

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**Ulcerative Colitis**

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● Ulcerative colitis. This condition causes long-lasting inflammation and sores (ulcers) in the innermost lining of your large intestine (colon) and rectum.

● Crohn's disease. This type of IBD is characterized by inflammation of the lining of the digestive tract, which often spreads deep into affected tissues. Both ulcerative colitis and Crohn's disease usually involve severe diarrhea, abdominal pain, fatigue and weight loss.

IBD can be debilitating and sometimes leads to life-threatening complications.

**What are the symptoms of IBD?**

**Some common symptoms are:**

* **Persistent diarrhea**
* **Abdominal pain**
* **Rectal bleeding/bloody stools**
* **Weight loss**
* **Fatigue**

**What causes IBD?**

The exact cause of IBD is unknown, but IBD is the result of a ***defective immune system***. In IBD, the immune system responds incorrectly to ***environmental*** triggers, which causes inflammation of the gastrointestinal tract. There also appears to be a ***genetic componen*t**—someone with a family history of IBD is more likely to develop this inappropriate immune response.

**IBD diagnosed?**

IBD is diagnosed using a combination of ***endoscopy*** (for Crohn’s disease) or ***colonoscopy*** (for ulcerative colitis) and ***imaging studies,*** such as contrast ***radiography***, ***magnetic resonance imaging (MRI), or computed tomography (CT)***.

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Physicians may also check stool samples to make sure symptoms are not being caused by an infection or run blood tests to help confirm the diagnosis.

**Crohn's Disease**

\*Crohn's disease is a type of inflammatory bowel disease (IBD) that may affect any segment of the gastrointestinal tract from the mouth to the anus. Crohn’s disease, also called regional enteritis or ileitis, is a lifelong form of inflammatory bowel disease (IBD).

\*Symptoms often include abdominal pain, diarrhea (which may be bloody if inflammation is severe), fever, abdominal distension, and weight loss. Crohn’s disease can cause diarrhea and stomach cramps. It’s common to experience periodic disease flare-ups..

**\*Other complications outside the gastrointestinal tract** may include anemia, skin rashes, arthritis, inflammation of the eye, and fatigue. The skin rashes may be due to infections as well as pyoderma gangrenosum or erythema nodosum Bowel obstruction may occur as a complication of chronic inflammation, and those with the disease are at greater risk of colon cancer and small bowel cancer.

\*While the precise causes of Crohn's disease are unknown, it is believed to be caused by a combination of environmental, immune, and bacterial factors in genetically susceptible individuals. It results in a chronic inflammatory disorder, in which the body's immune system defends the gastrointestinal tract, possibly targeting microbial antigens. It most commonly starts between the age of 13 and 30.

The condition inflames and irritates the [digestive tract](https://my.clevelandclinic.org/health/articles/7041-the-structure-and-function-of-the-digestive-system) — specifically the small and large intestines.

\***Location:** Crohn’s can affect any area from the mouth to the anus. It often affects ileum.

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\*Crohn’s disease gets its name from American gastroenterologist Dr. Burrill Crohn (1884-1983). He was one of the first physicians to describe the illness in 1932.

**The types of Crohn’s disease**

Crohn’s disease can affect different sections of the digestive tract. Types of Crohn’s disease include:

* **Ileocolitis:** Inflammation occurs in the small intestine and part of the large intestine, or colon. Ileocolitis is the most common type of Crohn’s disease.
* **Ileitis:** Swelling and inflammation develop in the small intestine (ileum).
* **Gastroduodenal:** Inflammation and irritation affect the stomach and the top of the small intestine (the duodenum).
* **Jejunoileitis:** Patchy areas of inflammation develop in the upper half of the small intestine (called the jejunum).

**Etiology**

\*The precise etiology of Crohn disease (CD) is unknown, but there are several known risk factors, **including family history, smoking, use of oral contraceptives, diet, and ethnicity.**

**\*** A combination of factors, **including aberrant mucosal immune responses, intestinal epithelial dysfunction, and defects of host interactions with intestinal microbes likely contribute to CD.**

\***1/Genetics**

\*There is a clear genetic predisposition for Crohn disease. First-degree

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relatives have a 13- 18% increase in incidence, and there are concordance rates of 50% in monozygotic twins.

\* Classic Mendelian inheritance is not seen, implying a polygenic basis of the disease. Molecular linkage analyses of affected families have identified NOD2 (nucleotide-binding domain 2) as a susceptibility gene in CD. NOD2 encodes a protein that binds to intracellular bacterial peptidoglycans, subsequently activates NF-kB (nuclear factor kappaB), and may be involved both in preventing excessive immune activation and in combating luminal microbes.

\*However, fewer than 10% of individuals carrying NOD2 mutations develop the disease, and genomic screening has identified linkage to multiple chromosomes, including chromosomes 3, 7, 12, and 16. **2/Environment**

\*Environmental factors, especially cigarette smoking and diet, are also clearly involved in this disease.

\*Tobacco smoking doubles the risk of both initial and recurrent Crohn disease (CD), unlike the apparent protective effect of tobacco seen in ulcerative colitis.

\*Improved food storage conditions and decreased food contamination may also contribute to the increase in incidence. This so-called "hygiene hypothesis" suggests that the reduction in enteric infections in developed countries has resulted in inadequate development of the regulatory processes that limit mucosal immune responses.

**3/Infective agents**

\*Given the success of treatment of peptic ulcer disease with the discovery of Helicobacter pylori as the causative agent, there have

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been multiple studies attempting to link an infectious agent with inflammatory bowel disease (IBD). Although decreased numbers of native lactobacilli and overgrowth of enteric bacteria are postulated to trigger excessive inflammation seen in Crohn disease (CD), a single causative infectious agent has not been identified.

\*Mycobacteria have been studied extensively in this context, given the histopathologic similarities between intestinal tuberculosis and CD, but the suggestion that mycobacteria play an etiologic role has been largely disputed.

**Symptoms**

Crohn's disease are due to inflammation in the wall of the affected parts of the gut (gastrointestinal tract). When the disease flares up, the inflammation may cause one or more of the following:

● Diarrhoea is the most common first symptom. It can vary from mild to severe. The diarrhoea may be mixed with mucus, pus or blood. An urgency to get to the toilet is common. A feeling of wanting to go to the toilet but with nothing to pass (tenesmus) is also common.

● Pain occurs in about 7 in 10 cases. The site of the pain depends on which part of the gut is affected. The last part of the small intestine (ileum) is the most common site. Therefore, a common area of pain is the lower right side of the tummy (abdomen). When Crohn's disease first develops it is sometimes mistaken for appendicitis. The severity

of pain can vary from person to person. Also, a sudden change or worsening of pain may indicate a complication.

● Weight loss that is not intentional is another common symptom.

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● Ulcers. An ulcer is a raw area of the lining of the gut which may bleed. You may see blood when you pass stools (faeces).

●Generally feeling unwell, which may include loss of appetite, high temperature (fever), and tiredness.

● Anaemia may occur if you lose a lot of blood.

● Mouth ulcers are common.

●Anal fissures may occur. These are painful cracks in the skin of the anus. Skin tags (small fleshy wart-like lumps) may also appear around the anus.

Symptoms can vary and depend on which part or parts of the gut are affected - for example:

●You may not have diarrhoea if the disease is just in the small intestine.

●A persistent pain in the abdomen without any other symptoms may be due to a small patch of Crohn's disease in the small intestine.

●A severe flare-up can make you generally very ill.

●If large parts of the gut are affected, you may not absorb food well and you may become deficient in vitamins and other nutrients.

**Other symptoms**

Other parts of the body are affected in some people in addition to the gut. These include:

● Inflammation and pain of some joints (arthritis).

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● Skin rashes.

● Inflammation of the middle layer of the eye (uveitis).

● Liver inflammation.

These problems can cause various symptoms.

It is not clear why these other problems occur. The immune system may trigger inflammation in other parts of the body when there is inflammation in the gut. These other problems tend to go when the gut symptoms settle, but not always.

**Pathophysiology**

Chronic inflammation from T-cell activation leading to tissue injury is implicated in the pathogenesis of Crohn disease. After activation by antigen presentation, unrestrained responses of type 1 T helper (Th1) cells predominate in Crohn disease as a consequence of defective regulation. Th1 cytokines such as interleukin (IL)-12 and TNF-α stimulate the inflammatory response. Inflammatory cells recruited by these cytokines release nonspecific inflammatory substances, including arachidonic acid metabolites, proteases, platelet activating factor, and free radicals, which result in direct injury to the intestine.

\* In a study from 2012, investigators suggested that genetic predispositions for inflammatory bowel disease (IBD) lead to abnormal epithelial barrier integrity and homeostasis, deficits in autophagy, deficiencies in innate pattern recognition receptors, and problems with lymphocyte differentiation, especially in Crohn disease.

(Microscopically, the initial lesion starts as a focal inflammatory infiltrate around the crypts, followed by ulceration of superficial mucosa. Later,

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inflammatory cells invade the deep mucosal layers and, in that process, begin to organize into noncaseating granulomas.

\*The granulomas extend through all layers of the intestinal wall and into the mesentery and the regional lymph nodes. Colonic granuloma in patient with Crohn disease.

\*Hematoxylin-eosin staining. Image courtesy of Dr E. Ruchelli. Neutrophil infiltration into the crypts forms crypt abscesses, leading to destruction of the crypt and atrophy of the colon. Chronic damage may be seen in the form of villous blunting in the small intestine as well. Ulcerations are common and are often seen on a background of normal mucosa.

\* Although granuloma formation is pathognomonic of Crohn disease, its absence does not exclude the diagnosis.

\*Macroscopically, the initial abnormality consists of hyperemia and edema of the involved mucosa. Later, discrete superficial ulcers form over lymphoid aggregates and are seen as red spots or mucosal depressions (see the image below). These can become deep, serpiginous ulcers located transversely and longitudinally over an inflamed mucosa, giving the mucosa a cobblestone appearance.

The lesions are often segmental, being separated by healthy areas, and are referred to as skip lesions.

**Diagnosing Crohn's Disease**

\* A series of tests can help diagnose Crohn's disease and rule out other conditions that may cause similar symptoms.

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\*Conditions with symptoms similar to those of Crohn's disease include:

● Irritable bowel syndrome (IBS)

● **Lactose intolerance**

● **Ulcerative colitis** (an inflammatory condition similar to Crohn's disease)

**Tests for Crohn's disease include:**

**\*Physical examination** the doctor will check for abdominal tenderness or pain.

* **\*Lab tests** the doctor may take

**Blood tests**

**\*A complete blood count** may reveal anemia, which commonly is caused by blood loss leading to iron deficiency or by vitamin B12 deficiency, usually caused by ileal disease impairing vitamin B12 absorption, and checks for high numbers of white blood cells that may indicate inflammation or infection.

\*Rarely autoimmune hemolysis may occur.

\* Ferritin levels help assess if iron deficiency is contributing to the anemia.

**\*Erythrocyte sedimentation rate (ESR) and C-reactive protein** help assess the degree of inflammation, which is important as ferritin can also be raised in inflammation.

**\*Serum iron,** **total iron binding capacity and transferrin saturation may be more easily interpreted in inflammation.**

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\*Anemia of chronic disease results in a normocytic anemia.

**\*Low serum levels of vitamin D are associated with Crohn's disease. .**

\***Testing for Saccharomyces cerevisiae antibodies (ASCA) and anti -neutrophil cytoplasmic antibodies (ANCA)** has been evaluated to identify inflammatory diseases of the intestine and to differentiate Crohn's disease from ulcerative colitis.

* **Stool test:** This test to check for bacteria or parasites. It can rule out infections that cause chronic diarrhea.

\*Lab tests can also help rule out other conditions.

* **Colonoscopy:**During a [colonoscopy](https://my.clevelandclinic.org/health/diagnostics/4949-colonoscopy), to examine the inside of the colon. With a tissue sample ([biopsy](https://my.clevelandclinic.org/health/diagnostics/15458-biopsy-overview)) from the colon to test for signs of inflammation.
* \***Imaging tests** **Computed tomography (CT) scan:** A [CT scan](https://my.clevelandclinic.org/health/diagnostics/4808-computed-tomography-ct-scan) creates images of the digestive tract. To show how severe the intestinal inflammation is. Wireless capsule endoscopy. You'll swallow a capsule containing a tiny video camera (about the size of a large vitamin) that allows doctors to see abnormalities throughout your digestive tract
* **Upper gastrointestinal (GI) endoscopy:**
* **Upper gastrointestinal (GI) exam:** X-ray images used to watch as a swallowed barium liquid moves through the digestive tract

**Treatment**

Treatment for Crohn’s disease varies depending on what’s causing the symptoms and how severe they are.

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\*In children, the goal in treatment is to induce remission (the time between symptom flare-ups), maintain remission and manage any complications of Crohn’s disease over time. one or more of these treatments for Crohn's disease may recomanded:

* **Antibiotics:** Antibiotics can prevent or treat infections. Severe infections can lead to abscesses (pockets of pus). Or they can cause [fistulas](https://my.clevelandclinic.org/health/diseases/14466-anal-fistula) (openings or tunnels that connect two organs that don’t normally connect).
* **Antidiarrheal medication:**  can stop severe diarrhea.
* **Biologics:**
* **Bowel rest:**To give the intestines a chance to heal, may recommend going without food or drink for several days or longer.
* To get the nutrition need, subject may receive intravenous (parenteral) nutrition. Only drink a prescribed liquid or have a [feeding tube](https://my.clevelandclinic.org/health/treatments/21098-tube-feeding--enteral-nutrition) during this time.
* **Corticosteroids:** Cortisone, prednisone and other [corticosteroids](https://my.clevelandclinic.org/health/drugs/4812-corticosteroids) ease inflammation brought on by autoimmune disease.
* **Immunomodulators:**These drugs calm inflammation by suppressing an overactive immune system. They include azathioprine and cyclosporine.
* **Surgery:** Surgery won’t cure Crohn’s disease, but it can treat complications. Subject may need surgery to correct intestinal perforations (holes), blockages or bleeding.

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**Complications of Crohn’s disease**

Crohn’s disease can lead to serious complications, including: **Abscesses:**Infected pus-filled pockets form in the digestive tract or abdomen.

* **Anal fissures:**Small tears in the anus ([anal fissures](https://my.clevelandclinic.org/health/diseases/13177-anal-fissures)) can cause pain, itching and bleeding.
* **Bowel obstructions:** Scar tissue from inflammation, fistulas or a narrowed intestine can block the bowel partially or completely.
* Waste matter and gases build up. A blockage in the [small bowel](https://my.clevelandclinic.org/health/diseases/15850-small-bowel-obstruction) or [large bowel](https://my.clevelandclinic.org/health/diseases/15287-large-bowel-intestinal-obstruction) requires surgery.
* **Colon cancer:**Crohn’s disease in the large intestine increases the risk of [colon cancer](https://my.clevelandclinic.org/health/diseases/16878-colon-cancer).
* **Fistulas:** IBD can cause abnormal tunnel-like openings, called fistulas, to form in the intestinal walls. These fistulas sometimes become infected.
* **Malnutrition:**Chronic diarrhea can make it hard for the body to absorb nutrients. One common problem in people with Crohn’s disease is a lack of iron. Too little iron can lead to [anemia](https://my.clevelandclinic.org/health/diseases/3929-anemia) (low red blood cell count) when the organs can’t get enough oxygen.
* **Ulcers:** Open sores called ulcers can form in the mouth, [stomach](https://my.clevelandclinic.org/health/diseases/10350-peptic-ulcer-disease) or [rectum](https://my.clevelandclinic.org/health/diseases/21189-rectal-ulcers).

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