Crohn’s disease and its associated disorders
Crohn’s disease and its associated disorders

Prof. Dr. Volker Gross
Author
Prof. Dr. Volker Gross
Klinikum St. Marien
Medizinische Klinik II
Mariahilfbergweg 7
D-92224 Amberg
Germany
E-mail: gross.volker@klinikum-amberg.de
Contents

Diagnosis: Crohn's disease – what does it mean? 4
The symptoms of Crohn’s disease 7
Crohn’s disease and disorders of other organs 8
The role of the immune system 10
Crohn’s disease can affect the nervous system 12
Effects on the joints 14
Osteoporosis 16
Disorders of the eyes 17
Skin changes in Crohn’s disease 18
Liver, gallbladder and pancreas in Crohn’s disease 20
Crohn’s disease and renal disorders 22
The respiratory tract in Crohn’s disease 24
Psychic factors in Crohn’s disease 25
The risk of cancer in Crohn’s disease 28
Living with Crohn’s disease 29
Crohn’s disease and pregnancy 31
Nutritional requirements in Crohn's disease 32
Medical treatment of Crohn’s disease 34
Glossary 37
Diagnosis: Crohn’s disease – what does it mean?

Crohn’s disease takes it name from Dr. Burrill B. Crohn, a physician in New York, who in 1932 first described an inflammation of the small intestine that is chronic and results in formation of scar tissue in the bowel. The preferred site of this inflammation is the terminal (final) segment of the small bowel, which is also known as the ileum; hence, the disease has also been termed...
terminal ileitis. Crohn’s disease can strike at any age, even in infants and small children. Usually, however, the disease makes its first appearance in young adulthood (20–40 years of age).

Children affected by Crohn’s disease should be carefully treated as soon as the diagnosis is confirmed. If the disease is not recognized early, the untreated inflammation of the bowel can lead to growth retardation, delayed puberty and decreased levels of performance at school. In principle, practically the entire gastrointestinal tract can be affected by Crohn’s disease. Inflammatory changes affecting individual bowel segments are characteristic: these segments are separated by segments that are essentially normal.

The inflammation can affect all layers of the bowel wall, including the mucosal layer, the longitudinal (lengthwise) and annular (ring-shaped) muscles of the bowel wall and even the connective tissue that envelopes the bowel. The inflammatory changes in these tissues also affect the glandular structures of the bowel with the result that the digestive functions of the bowel are increasingly affected. The absorption of nutrients in the food and the secretion into the lumen of the bowel of substances necessary for normal digestion may both be compromised.

Once the acute inflammation has passed, scars and thickening of the bowel wall may remain in the affected bowel segments. The bowel lumen becomes more narrow and transport of food through the bowel is impeded.
Intestinal villi
Blood and lymphatic vessels

Mucosal folds, schematic

Normal intestinal villus
Inflammation
Fistula

Intestinal mucosa affected by Crohn’s disease
The informed patient

The symptoms of Crohn’s disease

In many cases, Crohn’s disease develops slowly and causes uncharacteristic symptoms. Patients usually complain of unclear abdominal pain and increased diarrhea. A more dramatic first presentation is, however, also possible, with very severe abdominal pain. Beside colicky abdominal pain, most patients with Crohn’s disease report recurrent diarrhea. There may also be irregular bouts of fever and persons affected by Crohn’s disease report unintended weight loss and depressed appetite.

The often unclear symptoms early in the course of the disease do not point directly to Crohn’s disease and it may sometimes take several years before the correct diagnosis is made. Laboratory evidence of inflammatory bowel disease include the unspecific signs of inflammation (accelerated erythrocyte sedimentation rate, an increase in the number of white blood cells and C-reactive protein and, in some cases, a decrease in the number of red blood cells). In other cases, the simultaneous occurrence of abdominal pain, diarrhea, fever, joint complaints, dermatitis (skin inflammation) and/or repeated inflammation of the eyes may be considered a sign of Crohn’s disease. Anal fistulae also point to Crohn’s disease.

The course of the disease is not continuous. Instead, Crohn’s disease occurs episodically in flares, separated by symptom-free intervals of varying length.
Crohn’s disease and disorders of other organs

The effects of Crohn’s disease are not confined to the bowel. In a high percentage of patients other organs and organ systems are affected, sometimes to such an extent that the underlying disease may actually be obscured. And, because Crohn’s disease is usually treated by the patient’s family physician, internist or gastroenterologist, changes in other organs can easily be missed.

Organs that may be affected by disorders accompanying Crohn’s disease

- Central nervous system
- Eye
- Lung
- Liver
- Biliary tract
- Joints
- Pancreas
- Kidney
- Skin
It is clearly in the patient’s own interest to pay special attention to changes in the skin, joints or eyes and ask his physician about the potential connection of changes in these organs to his bowel disease.

In rare cases, patients with Crohn’s disease may also exhibit changes in the pancreas, a gland in the abdomen responsible for providing the bowel with enzymes and other secretions necessary for normal digestion. Other patients may develop disorders of the respiratory tract, of the kidneys or even of the nervous system. It is even possible for more than one organ or organ system to be involved in the disease process. In some patients, a disorder affecting some organ or organ system may become so prominent that it obscures the symptoms of the underlying disease. Possibly, the work-up of this symptom will provide the detour necessary to identify the patient’s underlying inflammatory bowel disease. Clinical experience suggests that these accompanying disorders all have a common cause. This cause, however, is to be sought, not in the bowel, but in a disorder of the immune system. Certain arguments suggest that some of the disorders associated with Crohn’s disease may actually be due to the medical treatment of this disease. Researchers, however, are in agreement that the commonly encountered findings in various organ systems in patients with Crohn’s disease are caused by disturbances in the interplay of the various components of the immune system, the psyche, organic changes and drug treatment.
The role of the immune system

Researchers still cannot answer the question of why certain people develop Crohn’s disease. Evidence is mounting, however, that genetic predisposition, environmental factors and the immune system are involved in its development. About 25% of Crohn’s cases in Europe appear to be related to a defect in the so-called NOD2 gene.

Were one to spread it out flat, the entire surface area of the human digestive system would cover 200 to 300 m². This fact becomes even more important when one considers the enormous number and amount of substances with which it comes into contact on a daily basis through the food, many of which have the potential for causing serious disease. The digestive system serves as an interface between the body’s own environment and the outer world around it: to help protect this boundary, the digestive organs are furnished with a large number of different immunologically active cells. These belong to a group of cells that actively prevent the penetration of foreign proteins and other substances into the organism. In patients with Crohn’s disease, these immune cells are present in unusually large numbers and are activated. In this state, they produce an excess of pro-inflammatory substances (e.g. cytokines, chemical messengers). This can be corrected, at least in part, by drugs such as the corticosteroids or 5-aminosalicylic acid.

Immunoglobulin A (IgA) also plays an important role in the immune defences of the bowel; its function differs in several important ways from the more well-known immunoglobulin G (IgG), which is present predominantly in the blood. Studies have shown that, in patients in an active flare of inflammatory bowel disease, the relationship between IgA and IgG is shifted in favor of IgG. While IgA is primarily involved in keeping antigens away
from the bowel wall and preventing their entry into the body, IgG does not possess this capacity. Instead, it actually binds antigens to the bowel wall and this can contribute to inflammation and destruction of tissue.

Immunoglobulins of the G-class forming together with antigens and antibodies the so-called immune complexes may also be important for the development of disorders of other organs observed in patients with Crohn’s disease. These protein conglomerates pass through the body and leave behind damage of various types in many different organs.
Crohn’s disease can affect the nervous system

Some patients with Crohn’s disease and with ulcerative colitis, which is another type of inflammatory bowel disease, have suffered disturbances of circulation and even occlusion of small blood vessels affecting the central nervous system. Possible causes include changes in the viscosity or ability of the blood to flow, which may be due to fluid losses or to the presence of end products of inflammation in the blood, or to a local inflammation of the blood vessels in the brain. Because patients with Crohn’s disease often fail to absorb B vitamins in sufficient quantities, they may experience a vitamin deficiency, which, in turn, can cause damage to the nerves. An inflamed bowel segment or a surgically shortened bowel may not be able to absorb adequate amounts of vitamins and other nutrients from the food.
and provide them to the organism. Especially affected are the fat-soluble vitamins (A, D, E and K) and water-soluble vitamins of the B group (B₆ and B₁₂).

Some Crohn’s patients suffer from so-called polyneuropathies. This term indicates abnormal function of several nerves resulting in changes in sensitivity in the areas served by the affected nerves. Patients may notice reduced sensitivity or even stabbing pain, together with reduced activity of normal reflexes.

Patients with Crohn’s disease, who, due to the pronounced nature of their disease require treatment with metronidazole, may also suffer from nerve damage. Metronidazole fights bacteria in the bowel and can sometimes prevent worsening of the disease. The drug, however, also binds B vitamins and this may result in polyneuropathy with unpleasant sensations in the hands and feet or loss of reflexes. These symptoms usually resolve once metronidazole is discontinued.
Effects on the joints

Arthritis and Crohn’s disease can affect each other. Arthritic joint inflammation may occur in association with Crohn’s disease. The use of anti-inflammatory medications or analgesics (pain medication), such as aspirin, however, may make the symptoms of Crohn’s disease worse or provoke a flare. In such cases, the cooperation of two physicians from different areas of specialization may be necessary.

The causes for this simultaneous occurrence of inflammation in the joints and the bowel are believed to be immunological in nature. In some cases, antibodies directed at the body’s own tissues (autoantibodies, autoaggression) may be produced or may be induced by an inflammatory process due to infection. Such antibodies may damage tissue at any place they may be deposited.
Recent research has shown that the permeability (extent to which the bowel wall allows substances to pass) of the bowel in Crohn’s disease is increased, permitting abnormally large amounts of foreign substances to pass into the body and potentially stimulate the immune system. Pain in the large joints of the arms and legs and/or in the spinal column is reported by 25% of patients with Crohn’s disease. In some cases, the tendons and ligaments throughout the skeletal system may be painfully affected.

The close association between inflammation of the bowel and the joints is very apparent during treatment. Improvement in arthritic complaints may occur parallel to successful treatment and resolution of inflammatory activity in the bowel. One must not forget, however, that the severity of the joint inflammation does not always correlate to the intensity of the bowel inflammation. Similarly, the findings of endoscopy and a patient’s reported general condition may be highly contradictory.
Osteoporosis

Often, patients with Crohn’s disease exhibit a reduction in bone density. This condition is known as osteoporosis and can lead to fractures, especially in the spine. Particularly at risk are patients with chronic disease activity, poor nutritional condition, patients who have taken cortisone for extended periods, and those in whom significant sections of the small bowel have been surgically removed. Patients at risk for osteoporosis are advised to take calcium and vitamin D in order to stop further bone loss. In cases of very extensive osteoporosis, patients may benefit from bisphosphonates, which are drugs that inhibit bone destruction.
Disorders of the eyes

Inflammation of the eyes is reported in a much higher percentage of patients with Crohn’s disease than in the general population. Types of inflammation include conjunctivitis, an inflammation of the membrane surrounding the eyes; scleritis, an inflammation of the white of the eyes; iridocyclitis, an inflammation of the iris; uveitis, an inflammation of the middle layer of the bulb of the eye; and retinitis, an inflammation of the inner layer of the eye, which is immediately involved in vision. Most commonly associated with Crohn’s disease are inflammations of the sclera or iris and occur at first disease manifestation or in association with an acute flare. Patients complain of feeling a foreign body in the eye, and report pain, sensitivity to light and loss of visual acuity. These symptoms can be isolated or occur together. Therapy consists of cortisone eye drops and adequate treatment of the underlying bowel inflammation. It is very probable that these disorders of the eyes occurring in association to Crohn’s disease are due to an antigen-antibody reaction. It is important for both the patient and physician to consider an association between disorders of the eyes and Crohn’s disease in order that prompt referral to an ophthalmologist can be made at the first appearance of symptoms.
Skin changes in Crohn’s disease

Patients with Crohn’s disease not infrequently experience changes of the skin and the mucous membranes of the mouth and other areas. The mucous membrane of the mouth or the anal region may develop painful, reddened lesions, which, in some cases, are seen prior to the manifestation of the bowel disease and present a helpful clue pointing toward Crohn’s disease. Skin or mucosal lesions occur in up to 40% of patients with Crohn’s disease.

Dermatologists call these changes “granulomatous inflammation” because these nodular (knot-like) skin changes consist of characteristic cells of the immune system, including granulocytes, lymphocytes and monocytes. These more or less sharply demarcated, brownish to bluish red areas may in some cases be covered by a flaking crust. They are particularly common in the vicinity of fistulae or may be found where skin rubs against skin, such as under the breasts or in the groin.

Although they have no direct contact with the intestinal tract, such granulomatous lesions may occur on the inner sides of the lips or cheeks. In these areas, there may be characteristic cobble-stone-like thickening or painful fissures of the edge of the tongue.

Patients may sometimes develop painful, reddish nodules on the front side of their legs. This condition is called erythema nodosum. In some cases, purulent skin ulcerations may develop (pyoderma gangraenosum). These vary in size from millimeters to several centimeters and are not due to infection by pathological organisms.

Here, too, scientists believe that immunological damage to the skin and blood vessels in the skin underlies these lesions.
Some of the skin changes appear to be associated with the inadequate absorption of vitamins and trace elements caused by patients’ frequent diarrhea and loss of blood and fluid. For example, anemia may be associated with glossitis, an inflammation of the tongue, which manifests itself as a reddened and smooth tongue. Eczema-like changes around the mouth are due to zinc deficiency. Zinc is an important trace element crucial for the body’s immune defenses. Deficiencies in zinc may also result in prolonged healing of skin injuries. Similarly, skin fungi can more easily spread in persons whose immune systems have become weaker.
Liver, gallbladder and pancreas in Crohn’s disease

In rare cases, inflammation involving the liver and biliary system may also be observed. Such disorders are identified using blood tests to measure the levels of enzymes specific to the liver. In some cases, nodular conglomerations of cells (granulomas) may develop in the liver tissue. This condition is known as granulomatous hepatitis. These granulomas are similar to lesions seen in the mucosal membrane of the bowel in patients with Crohn’s disease.

The bile ducts may also be affected by a non-infectious inflammation (primary sclerosing cholangitis). The tissue that makes up the bile ducts may, as a result of inflammation, become hardened, while the ducts themselves may become narrowed (stenosis). This acts to impede the flow of bile and this back-up can, on one hand, damage the liver, while, on the other, patients are at a higher risk of developing gallstones. These stones have a tendency to form or become trapped at narrow points in the bile ducts, resulting in an increase in the symptoms of biliary stasis, or can cause patients to experience biliary colic.

Patients with Crohn’s disease can also develop different types of problems with the pancreas. For example, in very rare cases, drugs used to treat Crohn’s disease (sulfasalazine, mesalazine, azathioprine) have been known to cause acute pancreatitis, or inflammation of the pancreas.

Acute pancreatitis, however, may also occur as one of the so-called extraintestinal manifestations (effects of the disease occurring outside the bowel) of Crohn’s disease. This may be due to changes in the duodenum, the first segment of the small bowel after the stomach. The pancreas produces important digestive enzymes...
and secretes these through a small duct into the duo-
denum. Inflammatory narrowing or occlusion of this
duct may result in a back-up of secretions in the pan-
creas.

The altered secretion of digestive enzymes seen in
some patients with Crohn’s disease is thought to be
due to the general disturbance of digestion in the affect-
ed bowel segments or to an immunological cause. The
occurrence of elevated pancreatic enzyme levels in the
serum, especially of $\alpha$-amylase (which may often be
independent of acute bowel inflammation and without
any other complaints) is, by itself, no sign of acute pan-
creatitis. Acute pancreatitis manifests itself as severe
upper abdominal pain associated with elevation of all
pancreatic enzymes (amylase, lipase) in the blood.
Crohn’s disease and renal disorders

Crohn’s patients have an increased risk of nephrolithiasis (development of kidney stones). An important cause of this phenomenon is believed to be the increased absorption of oxalic acid in the damaged bowel segments. Kidney function, however, may also be reduced by the development of amyloidosis, which is a condition in which a certain type of protein (amyloid) is deposited in the kidneys. The increased precipitation of immune complexes in the renal tubules has also been discussed as a cause for damage to the kidneys and the resulting loss of renal function. Patients experience the increased loss of protein in the urine, probably due to damage to the membrane of the renal tubules caused by substances related to inflammation, such as tumor necrosis factor (TNF). This damage permits large protein molecules to pass from the blood into the urine. Because of the losses of large amounts of fluid through the bowel, the body loses important molecules known as electrolytes (sodium, bicarbonate). This causes a
shift in the balance of the electrolytes. This mechanism may also be responsible for the development of kidney stones.
A very rare complication of the treatment of Crohn’s disease is the development of nephritis, or inflammation of the kidneys. The cause of this is believed to be an intolerance or allergy to the anti-inflammatory medication.
The respiratory tract in Crohn’s disease

It is highly probable that immunological processes, such as those believed to occur in Crohn’s disease, also cause changes in the respiratory tract. In fact, many Crohn’s patients do exhibit mildly reduced pulmonary function, but the effects can be quite variable. For example, in some patients, the trachea and bronchi may be inflamed or reduced in caliber. Other patients may experience an allergy-like disorder of the lung tissue (alveolitis), in which the alveoli (the tiny sacs in the lungs where gas exchange take place) are inflamed; or the pleural membrane, which envelops the lungs, may be affected. Because these disorders are extremely rare concomitants of Crohn’s disease, it has not yet been possible to demonstrate a clear association with disease activity or with the duration of the disease. To complicate matters further, the drugs used to treat Crohn’s disease can also cause allergic or inflammatory reactions in the lungs. Especially at risk are patients in whom pulmonary function has already been compromised by the inflammatory bowel disease.
Psychic factors in Crohn’s disease

It has only been in the last few years that researchers have identified an association between changes in the nerves and psychic reactions. It has been shown, for example, that the so-called vegetative nervous system (comprised of the sympathetic and parasympathetic nervous systems) can exert both stimulating and inhibitory effects on the immune system. Of interest to the researchers was the observation that not only do the nerve cells of the brain (the central nervous system) possess regulatory influences over the immune system but that information from the immune system reaches the nerves and the brain. The brain regulates the production of important hormones, including the corticosteroids, growth hormones and the sex hormones. An antigen-antibody reaction as a response of the immune system is also affected by this system through the increased production of glucocorticoids. This is the basis of the body’s own counter-reaction to self-immunization. Also involved in this process are the cytokines, substances involved in the transfer of information between inflammatory cells (lymphocytes, monocytes). Feedback control of the body’s own immune response regulates the extent and duration of each individual immune reaction.

Of high scientific interest are the reactions of the human immune system to psychic stress. Information in this regard has been collected from patients who suffer from depression, people who have recently lost their spouses, and others exposed to significant psychic stress. The association of psychic and immunological processes represents a complex network of biochemical, neuro-hormonal and immunological components, each of which exerts an effect on the psychological state and on the immune system of patients with Crohn’s disease.
To this category belong the many cases in which exposure to psychic stress has been followed by a worsening of patients’ inflammatory bowel disease. Conversely, however, solving a psychic problem may be associated with improvement in patients’ inflammatory bowel symptoms.
Psychotherapy can be an important tool for solving psychic conflicts and may at the same time help in reducing the symptoms of inflammatory bowel disease. Psychotherapeutic counseling, autogenic training, deep relaxation and physiotherapy in either individual or group setting can in many cases result in improvement in physical symptoms when instituted as an adjuvant psychological therapy.
The risk of cancer in Crohn’s disease

Patients with Crohn’s disease affecting the colon (large bowel) have an increased risk of developing cancer of the colon when the duration of their disease exceeds 10 years. The risk continues to rise in proportion to the duration of the disease. For this reason, patients with extensive Crohn’s disease for more than eight years should undergo colonoscopy every one to two years. This allows for early detection of any developing colon carcinoma and increases the prospects for curative surgical therapy.

There is evidence that consequent treatment with sulfasalazine or 5-aminosalicylic acid significantly reduces the risk of developing cancer of the colon.
Living with Crohn’s disease

Inflammatory bowel diseases – this includes Crohn’s disease and ulcerative colitis – are disorders that have not yet been fully understood. For this reason, there is no therapy which can truly be said to address the cause of these diseases. The therapeutic alliance between physician and patient is characterized by the subjective experience of the patient and the knowledge and experience of the treating physician. Not infrequently, there may be a difference between the objective assessment of the physician and the patient’s subjective experience of his disease. And each patient has experienced phases of life when he has the strength to more fully tolerate and accept his disease, as well as more stressful phases, when the ability to master the situation may be completely lost.

As long as there are no reliable methods of cure, therapy must remain limited to improving the symptoms and preventing or managing any complications of the disease that may occur. Changes in diet, a large number of drugs of varying efficacy, and psychological and surgical treatments represent the spectrum of possible therapies. Whether conservative methods are instituted singly or to complement one another, and whether surgery will ever be required must be decided in close cooperation between physician and patient.

Of especial assistance to the patient are the many self-help groups that have been formed in many areas. These groups provide a setting for people with similar problems to meet and exchange experiences, express their feelings, pass on recommendations on correct behavior, diet, and much more. Most importantly, they deal with the problems of the disease from a position of understanding and support.
Physician, family and self-help group belong to the close social environment of patients with Crohn’s disease. Frank discussions and cooperation in developing coping strategies not only assist the Crohn’s patient to accept the fact that he suffers from a chronic disease but also help persons in the patient’s social environment to better understand both the patient and his specific issues.
Crohn’s disease and pregnancy

Crohn’s disease can manifest itself at any age; hence, women of childbearing age may also be affected. Concerns that the disease may have a negative impact on the course of pregnancy, however, have not been confirmed. Long-term observations of pregnant women with Crohn’s disease, in fact, suggest that the severity of the disease may actually improve during pregnancy. This may be related to the fact that the hormonal environment changes so profoundly during pregnancy. This observation is also supported by the fact that, in many patients, the dose of medications used to treat Crohn’s disease can be reduced. Should it happen, however, that the activity of the disease increases despite co-existing pregnancy, there are today a number of very effective drugs for reducing the inflammation of Crohn’s disease that are not associated with increased risks for the unborn child. Use of mesalazine (5-aminosalicylic acid), salazosulfapyridine and corticosteroids is not contraindicated in pregnancy. There is also much evidence that azathioprine does not negatively affect pregnancy.

A comparison of pregnant Crohn’s patients and pregnant women in the general population has shown that the probability of giving birth to a healthy baby is identical for both groups. In addition, the risk of Crohn’s patients for miscarriage or birth defects in the baby does not differ from that of the general population. Of particular importance is a close cooperation between the patient’s gynecologist and the internist or gastroenterologist who is managing the patient’s Crohn’s disease. This will help assure that any complications can be detected early and promptly treated.
Nutritional requirements in Crohn’s disease

There is no uniform diet that can be prescribed for all Crohn’s patients. However, some guidelines for proper nutrition have been proposed, which should help patients avoid mistakes in planning their nutrition. Cakes and foods with a high sugar content have been implicated in a worsening of Crohn’s symptoms in some patients. Foods that have the potential for causing large amounts of gas should also be avoided by Crohn’s patients. So-called dietary fiber plays an important role in supporting regular bowel function. Special care, however, is necessary in patients with scar tissue formation or inflammation, which has resulted in a narrowing of the bowel (stenoses). These patients must consume a diet low in dietary fiber.

It should be clear to both the physician and patient that nutritional deficits in the sense of a deficiency situation can occur during an acute flare of an inflammatory bowel disease. In particular, deficiency syndromes can arise for protein, lipids (fats), electrolytes, vitamins and trace elements. Depending on the acute or chronic course of the disease, these may have various causes:

A **protein deficiency** may occur if:
- The diet is too one-sided or if the patientfasts due to fear of symptoms.
- Nutrients are not adequately absorbed in bowel segments affected by inflammation.
- Inflammatory secretions with high protein content are lost through the bowel.
- Loss of protein through the kidneys if these are affected by the disease.
The informed patient

Iron deficiency is usually due to a loss of blood. However, chronic inflammation may also be characterized by a disorder of iron metabolism in which the transport of, and binding capacity for iron is reduced. Iron is an important element for blood production and is crucial for oxygen transport. Therefore, all patients with inflammatory bowel disease should have their iron levels checked on a yearly basis.

Vitamin deficiencies, especially deficiencies of fat-soluble vitamins (vitamins A, D, E and K), may be due to extensive inflammation affecting the small bowel or resection of significant portions of the small bowel, but also to inadequate diet, especially when the disease activity has become chronic. Especially important is a deficiency of vitamin D (risk of osteoporosis) and/or vitamin B₁₂ (anemia).

Disturbances of water and electrolyte metabolism are due to the high losses of fluid associated with watery diarrhea. Sodium, potassium, calcium and chloride are dissolved in every body fluid and are lost together with any loss of fluid. These losses, however, can be compensated by a supplementation of electrolytes with the diet or in the form of tablets or electrolyte drinks.

Trace elements such as magnesium, copper, selenium and zinc play important roles in different organs. Deficiencies of these substances can be determined at a yearly routine check of laboratory values and supplemented, if needed.
Medical treatment of Crohn’s disease

Drugs can be used both to treat an acute flare of Crohn’s disease (acute phase therapy) and to prevent recurrence of inflammation (remission maintenance).

“Cortisone” or better corticosteroids

“Cortisone” or, more correctly, corticosteroids represent a group of agents (prednisone, prednisolone, methyl-prednisolone etc.) that are among the most important drugs used to treat Crohn’s disease. Patients whose disease manifests itself as an isolated inflammation of the small bowel or as a combination of disease affecting both the small bowel and colon usually respond well to corticosteroids. In Crohn’s disease limited to the colon, however, their efficacy is often poorer. In acute disease flares, corticosteroids must be administered at a sufficiently high dose (e.g. prednisolone, 60 mg per day). If disease activity is reduced by this treatment, the dose can be slowly tapered. As disease activity decreases, the dose can be slowly reduced and the agent can be completely discontinued after about three months.

Budesonide

In an effort to find agents that preserve the high efficacy of corticosteroids but are not associated with the same degree of side effects, new kinds of corticosteroids have been developed. Among these new corticosteroids are some which are known as topical corticosteroids: these are drugs that work locally at the site of application. One of these, budesonide, has become an accepted treatment for patients with Crohn’s disease. Budesonide is effective after administration as a capsule, enema or rectal foam directly on the inflammation of the intestinal mucosa. The drug is also absorbed in the
bowel and carried by the circulation to the liver. Unlike other corticosteroids, however, about 90% of the absorbed budesonide is broken down in the liver to inactive substances: hence, only a tiny portion of the administered dose can be distributed in the body and cause side effects. Several large studies have shown that the efficacy of budesonide is only slightly less than that of conventional corticosteroids but is associated with a significantly lower rate of side effects. Budesonide, however, should not be used in patients with very severe disease activity, in those with extensive extraintestinal disease affecting other organs, or when Crohn’s lesions are present in the esophagus, stomach or duodenum, since the drug is not sufficiently effective at these sites.

**Salazosulfapyridine**
Salazosulfapyridine no longer plays a meaningful role in the treatment of Crohn’s disease. It is mostly used only in cases of joint disease associated with Crohn’s disease.

**Mesalazine/5-aminosalicylic acid (5-ASA)**
Mesalazine has replaced salazosulfapyridine in the treatment of Crohn’s disease. Mesalazine is particularly useful in treating a mild flare of Crohn’s disease, especially in the terminal ileum and colon. Mesalazine can also help prevent the occurrence of recurrent flares of Crohn’s disease. An advantage of the substance is its good tolerability. It is available in the form of tablets, enemas and suppositories.

**Azathioprine**
The most effective medication for long-term management of Crohn’s disease is azathioprine, which is especially useful in patients who are dependent on, or resistant to corticosteroids. Azathioprine, however, can also be successfully used to prevent disease recurrence (re-
mission maintenance). It is more potent than mesalazine, but, because of its greater strength, requires closer monitoring of the patient.

**Anti-TNF-α antibody**

Tumor necrosis factor-α (TNF-α) is a substance produced in the body that plays an important role in the inflammatory process associated with inflammatory bowel disease. The anti-TNF-α antibody, infliximab, causes the destruction of activated immune cells and, therefore, has immunosuppressive and anti-inflammatory effects. The antibody is administered as an intravenous infusion. It can be used in patients with Crohn’s disease that has proven resistant to conventional therapeutic measures. In some patients, administration of this antibody leads to rapid reduction in disease activity. This is also true for patients whose disease has been complicated by the development of fistulae. Administration of the antibody at eight-week intervals has also been shown to prevent disease recurrence in some patients. Factors limiting the feasibility of this method include infusion reactions and the occurrence of infections, including tuberculosis, as well as its high costs.

The objective of any treatment of Crohn’s disease is to relieve inflammation as effectively as possible. In addition, a combination of medical treatment, appropriate diet and, when necessary, psychological support, should result in postponing the recurrence of disease as long as possible, making acute disease flares less frequent.

Close cooperation between the physician and patient can help to get the disease activity of Crohn’s disease under control. By controlling symptoms, the patient can expect a fairly normal life with only a moderate restriction in quality of life.
**Glossary**

**Absorption:** process by which substances are taken in through the skin or mucous membranes or other tissues into the blood or lymphatic system

**5-Aminosalicylic acid (5-ASA):** active ingredient in salazosulfapyridine

**Amyloidosis:** deposition of a certain protein in the tissue and the resulting disorder of metabolism

**Arthritis:** inflammatory disorder of the joints

**Causal therapy:** therapy, which targets the actual cause of a disease

**Cholangitis:** inflammation of the bile ducts

**Conjunctivitis:** inflammation of the membrane connecting the eye to the socket

**Conservative therapy:** any non-surgical form of treatment (drugs, diet, physiotherapy etc.)

**Cortisone:** a drug used to treat Crohn’s disease with high disease activity and which has an anti-inflammatory effect

**Crohn:** Burril B. Crohn (born 1884), the first physician to describe regional ileitis as an independent disease entity

**CRP:** C-reactive protein: a marker of inflammation in the blood

**Cytokine:** messenger substance associated with inflammation

**Enzymes:** biocatalysts, which accelerate chemical reactions
Episcleritis: inflammation of the connective tissue between the sclera and conjunctiva of the eye

Erythema nodosum: acute inflammatory skin disease of the subcutaneous adipose (fatty) tissue

Erythrocyte sedimentation rate (ESR): rate at which red blood cells settle in blood that has been treated so as not to coagulate

Fistula: abnormal tubular tract between one diseased hollow organ and another or between such an organ and the body surface

Granuloma: typical nodular structure that develops as a response of the tissue to an inflammatory or other process

Ileitis, terminal: inflammation of the end portion of the small bowel; another term for regional Crohn’s disease

Immune system: complex system in higher animals which defends the body from foreign proteins and other substances

Iridocyclitis: inflammation of the iris and ciliary body of the eye

Lesion: site of damage or injury

Lumen, bowel: the interior of the bowel

Muscle reflex: contraction of a muscle in response to brief extension

Nephrolithiasis: kidney stone disease

Oligoarthritis: simultaneous inflammation of 2–4 large joints

Polyneuropathy: disorder of more than one peripheral nerve

Psyche: soul, mood
Retinitis: inflammation of the inner layer of the bulb of the eye

Salazosulfapyridine: compound consisting of 5-aminosalicylic acid and sulfapyridine

Secretion: release of fluid or of molecules from cells

Scleritis: inflammation of the sclera (the white) of the eye

Uveitis: inflammation of the middle layer of the bulb of the eye
Further information for patients with inflammatory bowel diseases:

- **Ulcerative colitis and Crohn’s disease**
  An overview of the diseases and their treatment
  68 pages (S80e)

- **Diet and Nutrition in Crohn’s Disease and Ulcerative Colitis**
  20 Questions – 20 Answers
  60 pages (S84e)

- **Crohn’s Disease, Ulcerative Colitis and Pregnancy**
  51 pages (S82e)

- **Corticosteroid therapy in inflammatory bowel diseases**
  28 pages (Bu80e)

These brochures can be ordered **free of charge** from Falk Foundation e.V. or the local Falk partner.

**FALK FOUNDATION e.V.**

Leinenweberstr. 5
79108 Freiburg
Germany

www.falkfoundation.com