

Chronic Recurrent Multifocal Osteomyelitis (CRMO) Chronic Non-bacterial Osteomyelitis (CNO)

What is chronic recurrent multifocal osteomyelitis?

Chronic recurrent multifocal osteomyelitis (CRMO) is a rare and serious disease. It involves inflammation of one or more bones that can be chronic. Symptoms can come and go. CRMO is treated by pediatric rheumatologists. Inflammation may start in one bone, but later develop in other bones. CRMO is sometimes called chronic non-bacterial osteomyelitis (CNO) by physicians and in publications. “Non-bacterial” means there is no bacterial infection. The disease is not always recurrent or multifocal in nature.

Inflammation is a normal process. It is the way our immune system protects our bodies from infections and germs. It causes pain, redness, and swelling. In CRMO/CNO, however, there is no infection. Instead, the immune system attacks normal bone causing inflammation. CRMO/CNO is classified as an autoinflammatory disease.

Some children with CRMO/CNO have an increased risk of developing psoriasis, inflammatory bowel disease (Crohn’s Disease or Ulcerative colitis), arthritis and eye disease (uveitis).

How is CRMO/CNO diagnosed?

CRMO/CNO is a “diagnosis of exclusion.” This means that other diseases must be ruled out before the diagnosis can be made because the bone changes can look like infection or cancer. Generally, many tests are required, such as blood tests, X-rays, bone scans, MRI, and often a bone biopsy. There is no one test to confirm the diagnosis of CRMO/CNO. Your doctor will decide which tests are needed to diagnose your child.

Magnetic resonance imaging (MRI) is a technique that uses a magnetic field and radio waves to create detailed images of the organs and tissues within the body. Whole body MRI is the preferred imaging tool used to monitor CRMO/CNO. If a whole body MRI is not available, an MRI of specific sites (such as an ankle or collarbone) or a bone scan may be done. A bone scan is nuclear imaging test that uses radioactive materials to highlight areas of abnormal bone. A bone scan is not as sensitive as an MRI but can give a whole-body picture as a baseline. A bone biopsy is a procedure where a sample of bone is removed and tested for cancer, infection, or other bone diseases.

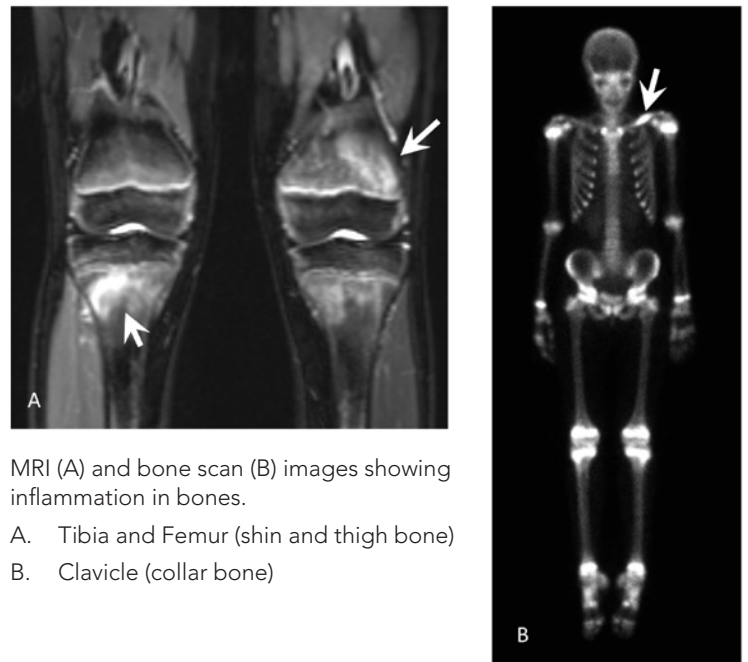
What causes CRMO/CNO?

The cause of CRMO/CNO is unknown. The immune system damages the bone. Genetic and environmental factors may play a role.

Images below are examples of inflammation within the bones of patients with CRMO/CNO.



A. Irregular area of bone destruction (indicated by arrow) in the right fibula (thinner bone of the ankle) shown on an X ray
 B. Normal left fibula from the same child on an X-ray



MRI (A) and bone scan (B) images showing inflammation in bones.

A. Tibia and Femur (shin and thigh bone)
 B. Clavicle (collar bone)

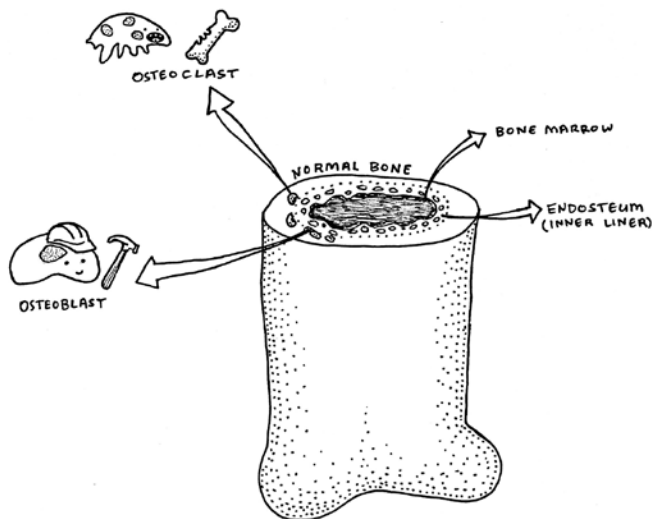
What is happening in the bone?

Your immune system cells produce proteins that send signals to make inflammation.

There are two main types of cells needed for bone development in children. One type of cell, osteoblasts, makes the bone. The other, osteoclasts, breaks down the bone. In normal bone development, these two cells work together to maintain healthy strong bones.

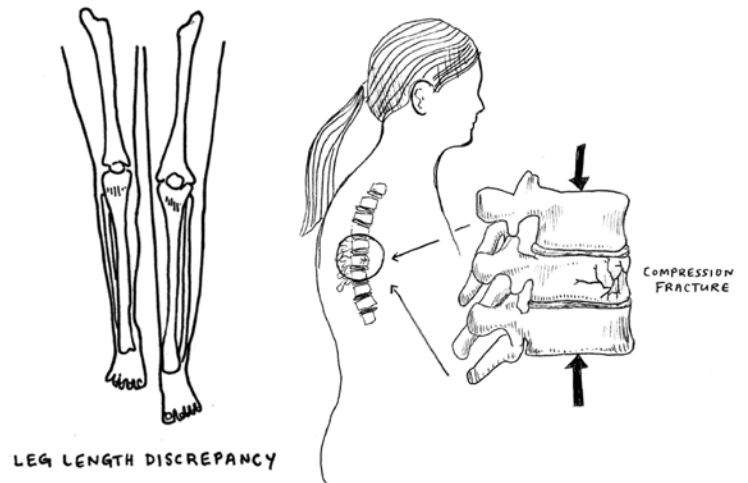
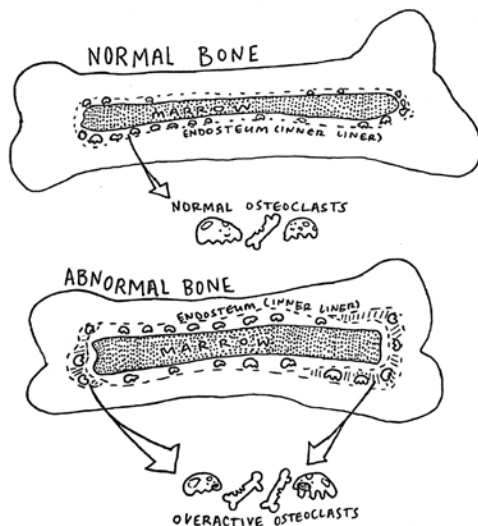
In CRMO/CNO, the immune system proteins make the osteoclasts work too much and the result is that they damage or eat the bone. This causes bone pain with or without swelling. Subsequently, fractures may occur. Even if the pain is better with treatment damage may still be occurring. Children with CRMO/CNO need long term follow up with a pediatric rheumatologist.

The drawing below illustrates normal and abnormal bone.



OSTEOBLASTS AND OSTEOCLASTS ARE CELLS THAT WORK TOGETHER TO MAKE BONE GROW.

OSTEOCLASTS BREAK DOWN OLD BONE, ALLOWING OSTEOBLASTS TO REPLACE IT WITH NEW BONE.



Illustrations by Lauren Potts

What happens after your child is diagnosed with CRMO/CNO?

Find a doctor who has experience with patients with CRMO/CNO. CRMO/CNO in children is generally treated by a pediatric rheumatologist. Ask your doctor for a referral.

Why do we treat CRMO/CNO?

- Reduce inflammation
- Prevent bone damage and bone deformities (for example fractures, leg length discrepancies, changes in the spine curvature)
- Help avoid growth problems
- Decrease pain

How is CRMO/CNO treated?

CRMO/CNO is different for each patient. Different children respond to different treatments. Your doctor may need to try several medications before finding the one that works for your child. In severe cases, doctors may combine medications to treat the disease. Your doctor will work with you and your child to help find the best treatment.

For some CRMO/CNO patients, the disease can be managed with nonsteroidal anti-inflammatory drugs (NSAIDs) alone. NSAIDs are the first-line treatment. NSAIDs work by blocking one of the signals that cause increased bone damage. This may decrease the pain and inflammation in the bone to allow normal growth.

Your physician may start additional medicines. Some of the reasons for that are the following:

- If NSAIDs alone are not effective
- If your child does not tolerate NSAIDs
- If there are high risk bone lesions, such as spinal lesions

In some cases, your doctor may use a short course of corticosteroids, for example, Prednisone (Deltason[®]) or Prednisolone (Orapred[®]).

These medicines are also used in children with other inflammatory and/or bone conditions. Side effects may occur while taking these medications. Your physician will have a discussion with you prior to starting any new treatment, which may include combination medications.

| NSAIDs | Additional Medications |
|--------------------------------------|---|
| Naproxen (Aleve [®]) | Methotrexate (Otrexup [®] , Rasuvo [®] , Trexall [®]) |
| Celecoxib (Celebrex [®]) | Sulfasalazine (Azulfidine [®]) |
| Meloxicam (Mobic [®]) | Leflunomide (Arava [®]) |
| Piroxicam (Feldene [®]) | Pamidronate (Aredia [®]) |
| Indomethacin (Indocin [®]) | Zoledronic Acid (Zometa [®] , Reclast [®]) |
| Diclofenac (Voltaren [®]) | Adalimumab (Humira [®]) |
| | Etanercept (Enbrel [®]) |
| | Infliximab (Remicade [®]) |

What happens after your child begins treatment?

Your child's pediatric rheumatologist will make sure your child gets the right care. CRMO/CNO is a chronic condition where symptoms can come and go for years. Children might have inflammation in other bones of the body without symptoms. For this reason, your doctor will want to see your child even if he/she is feeling well. Once your child is on effective treatment, he/she should begin to feel better.

The pediatric rheumatologist will carefully monitor your child. It is important to keep all appointments because your doctor will want to continue monitoring for bone inflammation and any problems with the medications.

Whole body MRI is an imaging tool used to monitor CRMO/CNO. If a whole body MRI is not available, your pediatric rheumatologist may order MRI of specific sites (such as an ankle or collar bone) or a bone scan. A bone scan is not as sensitive as an MRI but can give a whole-body picture as a baseline.

Having a new diagnosis of a chronic disease can be stressful. Your pediatric rheumatologist is available to suggest other resources for you and your child, which might include the following:

- Physical and occupational therapy for exercises to regain muscles strength and joint mobility, once your child has healed sufficiently.
- When disease is active, the therapy should be gentle. When the disease is controlled, therapy can be more intense.
- School accommodations, such as a 504 plan.

How will you and your doctor know whether a treatment is working?

- Decrease in pain
- Return to normal activities
- Improvement in inflammation tests and/or imaging studies

What is the prognosis for patients with CRMO/CNO?

Prognosis will depend on your child's individual disease and response to treatment. The course can be different depending on the child. Many children will not have active disease while on appropriate treatment, but in others, the disease may persist. Some children will need to stay on medications for many years and/or start additional medications. Others could come off medications. This is why it is important to continue seeing your pediatric rheumatologist.

Real Life Stories of Kids with CRMO

Marie got CRMO when she was three, but it was misdiagnosed as a sprain. She took Motrin with food for around three weeks, and soon felt fine. At age four, her ankle swelled and was hot and very painful. Fortunately Marie took Motrin with food for around six weeks, and felt fine. Marie's CRMO got a lot worse around age 10. Now Marie gets monthly infusions of an arthritis drug and is back to an active life. Unfortunately, because she did not get consistent care, she has a bone deformity that she will cope with for the rest of her life.

"I'm grateful to feel well. But I don't want everyone checking on me all the time. It takes medications to make sure I can lead a normal life, that's my normal."

Heidi got CRMO when she was only 18 months. Her parents were so relieved that it wasn't anything worse. When NSAIDs didn't work, Heidi began to get shots – given by her parents each week – and now lives an active life as a six year old!

"My parents think I'm brave and they worry about me. Watch me run, I'm the fastest!"

Alex got CRMO when he was 9. Fortunately NSAIDs have given Alex relief. But he never misses an appointment with his pediatric rheumatologist (who sees many other CRMO patients and keeps up with the news about CRMO). Alex is pain free and active.

"Seeing my CRMO doctor takes up a lot of my time, and that's a bummer, but that's my normal."

Bethany got CRMO when she was 15. Many adult rheumatologists have not seen patients with CRMO. Bethany's pediatric rheumatologist had a direct conversation with an adult rheumatologist to explain CRMO and review Bethany's health history.

"My treatments are expensive, but the hospital social worker helped me get financial assistance. I never miss an appointment because you only get one skeleton and I want to keep my bones in good shape!"

A CRMO parent speaks:

"It was terrifying when we learned that doctors needed to verify whether our daughter had cancer or a dangerous infection. When we learned it was CRMO instead, we really didn't understand anything about the disease or what it means to be a rare disease family and a family with a loved one who has a chronic condition. It has been an adjustment. Traveling to get care from someone who sees many patients with CRMO has made all the difference for us."

