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## **Chronic non-Bacterial Osteomyelitis/Osteitis (or CRMO)**

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### **1. WHAT IS CRMO**

#### **1.1 What is it?**

Chronic Recurrent Multifocal Osteomyelitis (CRMO) is the most severe form of Chronic Non-bacterial Osteomyelitis (CNO). In children and adolescents, the inflammatory lesions predominantly affect the metaphyses of the long bones of the lower limbs. However, lesions can occur at any site of the skeleton. Furthermore, other organs such as the skin, eyes, gastrointestinal tract and joints can be affected.

#### **1.2 How common is it?**

The frequency of this disease has not been studied in detail. Based on data from European national registries, approximately 1-5 of 10,000 inhabitants might be affected. There is no gender predominance.

#### **1.3 What are the causes of the disease?**

The causes are unknown. It is hypothesised that this disease is linked to a disturbance in the innate immune system. Rare diseases of bone metabolism might mimic CNO, such as hypophosphatasia, Camurati-Engelman syndrome, benign hyperostosis-pachydermoperiostosis and histiocytosis.

#### **1.4 Is it inherited?**

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Inheritance has not been proven but is hypothesized. In fact, only a minority of cases is familial.

### **1.5 Why does my child have this disease? Can it be prevented?**

The causes are unknown to date. Preventive measures are unknown.

### **1.6 Is it contagious or infectious?**

No, it is not. In recent analyses, no causative infectious agent (such as bacteria) has been found.

### **1.7 What are the main symptoms?**

Patients usually complain of bone or joint pain; therefore, the differential diagnosis includes juvenile idiopathic arthritis and bacterial osteomyelitis. Clinical examination may actually detect arthritis in a significant portion of patients. Local bone swelling and tenderness are common and limping or loss of function may be present. The disease can have a chronic or recurrent course. Skin lesions such as psoriasis, pustulosis and acne are often associated.

### **1.8 Is the disease the same in every child?**

It is not the same in every child. Moreover, the type of bone involvement, the duration and the severity of symptoms varies from patient to patient and even in the same child if a recurrent course is considered.

### **1.9 Is the disease in children different from the disease in adults?**

In general, CRMO in children resembles that seen in adults. However some features of the disease such as skin involvement (psoriasis, pustular acne) are more frequent in adults. In adults, the disease has been called SAPHO syndrome for synovitis, acne, pustulosis, hyperostosis and osteitis. CRMO has been considered the paediatric and adolescent version of SAPHO syndrome. SAPHO syndrome appears to

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have more spine, pelvis and chest wall involvements while metaphyses of the long bones are more often affected in CRMO.

3.1 How might the disease affect the child and the family's daily life? The child and the family experience joint and bone problems often over months before the disease is diagnosed. Admission to a hospital for further investigations before starting on treatment is usually recommended. Regular visits to an outpatient clinic for follow-up after the diagnosis are also recommended.

3.2 What about school? What about sports? There may be limitations for sport activities, especially after biopsy or if arthritis is present. Usually, there is no need to limit overall physical activity afterwards.

3.3 What about diet? There is no specific diet.

3.4 Can climate influence the course of the disease? No, it cannot.

3.5 Can the child be vaccinated? The child can be vaccinated, except with live vaccines when under treatment with corticosteroids, methotrexate or TNF- $\alpha$  inhibitors.

3.6 What about sexual life, pregnancy, birth control? Patients with CNO do not have fertility problems. In the event that the pelvic bones are affected, there may be discomfort in sexual activities. The need for medication must be re-evaluated before considering pregnancy and during pregnancy.