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Deficiency of IL-1 Receptor Antagonist (DIRA)

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1. WHAT IS DIRA

1.1 What is it?

Deficiency of IL-1Receptor Antagonist (DIRA) is a rare genetic disease. Affected children suffer from severe skin and bone inflammation. Other organs such as the lungs may be involved. Untreated, the disease may lead to severe disability and even death.

1.2 How common is it?

DIRA is very rare. Currently, less than 10 patients have been identified worldwide.

1.3 What are the causes of the disease?

DIRA is a genetic disease. The responsible gene is called IL1RN. It produces a protein, IL-1 Receptor antagonist (IL-1RA), that plays a role in the natural resolution of inflammation. IL-1RA neutralizes the protein interleukin-1 (IL-1), which is a powerful inflammatory messenger in the human body. If the IL1RN gene carries a mutation, as it does in DIRA, the body cannot produce IL-1RA. Therefore, IL-1 is no longer opposed and the patient will develop inflammation.

1.4 Is it inherited?

It is inherited as an autosomal recessive disease (which means that it is not linked to gender and that neither parent needs to show symptoms of the disease). This type of transmission means that to have DIRA, an

individual needs two mutated genes, one from the mother and the other from the father. Both parents are carriers (a carrier has only one mutated copy but not the disease) and not patients. Parents who have a child with DIRA have a 25% risk that a second child will have DIRA as well. Antenatal diagnosis is possible.

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

The child has the disease because it was born with the mutated genes that cause DIRA.

1.6 Is it infectious?

No, it is not.

1.7 What are the main symptoms?

The main symptoms of the disease are skin inflammation and bone inflammation. The skin inflammation is characterised by redness, pustules and scaling. The changes can affect every part of the body. Skin disease comes on spontaneously but it can be exacerbated by local injury. For instance, intravenous cannulae often lead to local inflammation. The bone inflammation is characterised by painful bony swellings, often with the overlying skin appearing reddened and warm. Many bones can be involved, including the limbs and the ribs. The inflammation typically involves the periosteum, the membrane covering the bone. The periosteum is very sensitive to pain. Therefore, affected children are often irritable and miserable. This may lead to poor feeding and impaired growth. Inflammation of the joint space is not typically a feature of DIRA. The nails of DIRA-patients can become deformed.

1.8 Is the disease the same in every child?

All affected children have been seriously ill. However, it is not the same in every child. Even within the same family, not every affected child will be equally ill.

1.9 Is the disease in children different from the disease in

adults?

DIRA has only been recognized in children. In the past, before effective treatment became available, these children would die before reaching adulthood. Hence, the features of DIRA in adulthood are unknown.