

NEMO

NEMO deficiency syndrome

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Supporting families affected
by primary and secondary
immunodeficiency

About this leaflet

This leaflet has been produced jointly between Immunodeficiency UK, Great Ormond Street Hospital (GOSH) and the Great North Children's Hospital. It explains the causes, symptoms and treatment of nuclear factor-kappa B essential modulator (NEMO) deficiency and where to get help. NEMO deficiency is a rare type of primary immunodeficiency.

The information has been reviewed by the Immunodeficiency UK Patient Representative Panel and by families affected by NEMO deficiency and endorsed by the Immunodeficiency UK Medical Panel. It should not, however, replace advice from a clinical immunologist or a geneticist.

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What is NEMO deficiency?

NEMO (nuclear factor-kappa B essential modulator) deficiency syndrome is a rare disorder and is often referred to simply as NEMO deficiency. It causes major abnormalities of the immune system but can affect many parts of the body, particularly the skin, hair, teeth and brain.

NEMO is a protein in white blood cells that signals infection. The protein is also present in other cells, such as the skin and teeth, where it is important in making the sweat glands, hair and normal-looking teeth. NEMO deficiency is one of a larger group of conditions known as primary immunodeficiencies. It is very variable in the symptoms it causes and how it progresses over time.

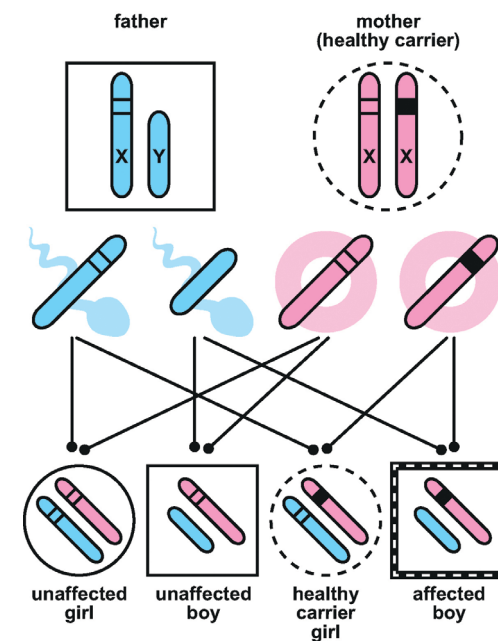
Another name for the condition is X-linked hypohydrotic ectodermal dysplasia and immunodeficiency (XL-EDA-ID).

What causes it?

NEMO deficiency is usually an inherited condition, passed on in families in the same way that physical characteristics, such as eye colour, are passed from parent to child. It is caused by a mutation (change) in a child's genetic make-up.

In boys with NEMO deficiency, one gene called *IKBKG* contains a spelling mistake (or mutation) that interferes with the normal function of the protein it makes, called NEMO. NEMO usually does an important job inside white blood cells as well as in the skin, where it is involved in developing teeth and hair.

As the *IKBKG* gene is located on the X chromosome, girls have a back-up copy so are very rarely affected. However, each time a female carrier has a baby boy, there is a 50 per cent chance her son will inherit the X chromosome bearing the mutated gene. This is called X-linked inheritance.



Mechanism of X-linked inheritance

Diagram: © UCL Health Creatives 2015

Sometimes new gene defects can occur 'out of the blue' in people with no history of the disorder in their family. If the genetic change occurs at the time of conception (in the eggs or sperm) it is called 'sporadic' and could be passed on to the next generation. If it occurs later in the development of the embryo, the gene mutation only affects blood cells and is called a 'somatic' variant. In this case, the genetic defect cannot be passed on to future generations.

Specialists in genetics and genetic counselling are on hand to talk through the inheritance of NEMO with you if needed. More information about genetics is also available in our separate leaflet available on our website at www.immunodeficiencyuk.org.

What are the signs and symptoms?

The first sign of NEMO deficiency is often a severe infection, such as meningitis or pneumonia, requiring hospital treatment and sometimes intensive care. Boys with NEMO deficiency are vulnerable to many types of germs because so many aspects of their immune system are impaired. The major culprits are bacteria called Pneumococci, relatives of tuberculosis (TB) called atypical mycobacteria and a fungus called Pneumocystis, but viral infections may also be a problem.

As well as being unable to fight infections as well as usual, the immune system may develop an 'autoimmune response' – that is, it starts to attack the body cells instead of foreign invaders, such as bacteria and viruses. If the autoimmune problems affects the guts it can cause diarrhoea and abdominal pain.

In NEMO deficiency, skin is usually very dry and thickened owing to of a lack of sweat glands. Hair is usually sparse. Teeth tend to have an unusual, round (conical) shape. This is called ectodermal dysplasia. Those affected may also develop multiple skin abscesses and a skin condition called molluscum contagiosum. Some boys may have swollen arms or legs owing to fluid retention (lymphoedema).

How is it diagnosed?

The most important step is recognising that there is a problem with the immune system and involving the right specialists to investigate further and determine treatment. The combination of skin and teeth abnormalities with severe infections can be very characteristic. Blood tests often show weak responses to vaccines and germs. They may also show signs of infection or autoimmune response. Genetic tests – also requiring a blood sample – will be needed to identify the mutation on the NEMO gene.

How is it treated?

The immediate priority is to diagnose and treat infection. Many boys have severe problems with their immunity and require complex treatment from an immunology specialist, possibly in hospital at first. Most patients will need antibiotics as well as immunoglobulin replacement treatment in the long term to prevent infection, but this can often be given at home. You can read more about immunoglobulin therapy in our related leaflet available on our website at www.immunodeficiencyuk.org.

Live vaccines should not be given to children with NEMO deficiency as they may be harmful. Regular monitoring and check-ups will help to catch infections early. If an autoimmune response occurs, this can be treated with steroid and/or other medicines to damp down the immune system, so relieving the symptoms. Skin complaints, such as eczema, may need to be managed.

In some severely affected patients, NEMO deficiency may need treatment using stem cell transplantation (HSCT). This is a fairly new treatment for NEMO deficiency, so its role is still being established. It is important to remember that a bone marrow transplant will resolve the problems with the immune system, but not the skin, teeth and hair. Studies are ongoing to understand better what this means in the long term. Information on HSCT can be found on our website at www.immunodeficiencyuk.org.

What does this mean for the future?

The outlook for children with NEMO deficiency is variable. With regular monitoring and prompt treatment of infections, some children can grow up to lead a near-normal life. Others may be more severely affected, suffering repeated and serious infections that can be life-limiting.

Is there a support group?

Immunodeficiency UK is the main support organisation in the UK for anyone affected by a primary or secondary immunodeficiency disease. Call our helpline on 0800 987 8986 or visit our website at www.immunodeficiencyuk.org.

Glossary

autoimmune an immune reaction against the body's own tissues. This can cause disease of organs (such as the thyroid gland), tissues (such as arthritis) or the blood. Autoimmune disease of the blood can lead to destruction of one or more types of blood cells – called haemolytic anaemia (destruction of red blood cells), thrombocytopenia (destruction of platelets, causing bleeding and bruising) or autoimmune neutropenia (destruction of neutrophils). These disorders can require urgent treatment. Many autoimmune diseases need treatments that suppress the immune system because of the damage they are causing, even though the immune system is weaker at fighting infections.

gene section of DNA on a chromosome that codes for a functional RNA molecule and thus a protein. Put another way, a word rather than a letter in the genetic code. Genes are the fundamental units of inheritance that carry the instructions for how the body grows and develops.

haematopoietic stem cell transplantation (HSCT) transfer of bone marrow (obtained by a medical procedure) or stem cells (obtained from blood or stored umbilical cord blood) from a donor – either related or unrelated – to a recipient. Haematopoietic means blood-forming. The donor cells are given by intravenous infusion and make their way to the recipient bone marrow to provide a new immune system, curing the immunodeficiency.

immunoglobulin proteins (globulins) in the body that act as antibodies. They work to protect against and fight off infections. They are produced by specialist white blood cells (plasma cells/B cells) and are present in blood serum and other body fluids. There are several different types (IgA, IgE, IgG and IgM), and these have different functions.

inheritance passing down of genetic information from parents to children.

lymphoedema swelling of lymphatic glands and vessels.

mutation a change in the structure of a gene or group of genes. Such changes can be passed on to the next generation. Many mutations cause no harm, but others can cause genetic disorders, such as primary immune deficiencies.

nuclear factor-kappa B essential modulator (NEMO) a protein that plays an important role in white blood cells as well as in the skin, the development of teeth and in the hair.

Notes

This image shows a blank sheet of white paper with horizontal ruling lines. The lines are evenly spaced and extend across the width of the page. There are no margins, text, or other markings on the paper.

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About Immunodeficiency UK

Immunodeficiency UK is a national organisation supporting individuals and families affected by primary and secondary immunodeficiency.

We are the UK national member of IPOPI, an association of national patient organisations dedicated to improving awareness, access to early diagnosis and optimal treatments for PID patients worldwide.

Our website has useful information on a range of conditions and topics, and explains the work we do to ensure the voice of patients with primary and secondary immunodeficiency is heard. If we can be of any help, please email us or call on the number above, where you can leave a message.

Support us by becoming a member of Immunodeficiency UK. It's free and easy to do via our website. Members get monthly bulletins.

Immunodeficiency UK is reliant on voluntary donations. To make a donation, please go to **www.immunodeficiencyuk.org/donate**



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