

NEMO

NEMO deficiency syndrome

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CHILDREN'S HOSPITAL

 **PID UK**
Supporting families affected
by primary immunodeficiencies

About this leaflet

This leaflet has been produced jointly between PID 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 PID UK Patient Representative Panel and by families affected by NEMO deficiency and endorsed by the PID 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.

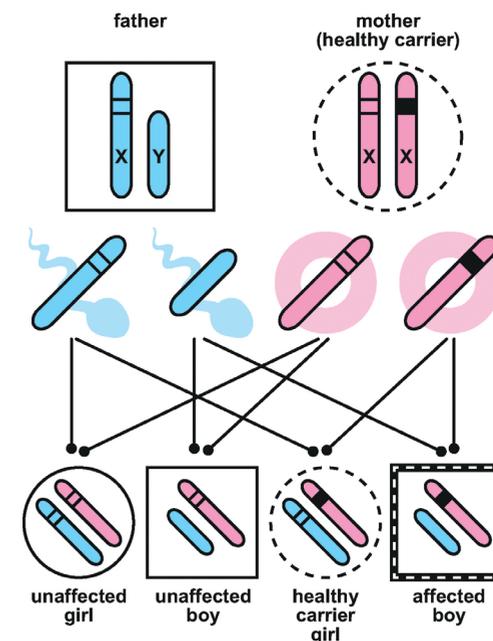
Another name for the condition is X-linked hypohydrotic ectodermal dysplasia and immunodeficiency (XL-EDA-ID).

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

www.piduk.org/static/media/up/geneticaspectsofpid.pdf.

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 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

www.piduk.org/static/media/up/lgguideforparents.pdf.

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 at

www.piduk.org/whatarepids/treatment/bonemarrowtransplantation.

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?

PID UK is the main support organisation in the UK for anyone affected by a primary immunodeficiency disease. Call their helpline on 0800 987 8986 or visit www.piduk.org.

About Primary Immunodeficiency UK

Primary Immunodeficiency UK (PID UK) is a national organisation supporting individuals and families affected by primary immunodeficiencies (PIDs).

We are the UK national member of the International Patient Organisation for Primary Immunodeficiencies (IPOP), an association of national patient organisations dedicated to improving awareness, access to early diagnosis and optimal treatments for PID patients worldwide.

Our website at www.piduk.org provides useful information on a range of conditions and topics, and explains the work we do to ensure the voice of PID patients is heard.

If we can be of any help, please contact us at hello@piduk.org or on **0800 987 8986**, where you can leave a message.

Support us by becoming a member of PID UK. It's free and easy to do via our website at www.piduk.org/register or just get in touch with us. Members get monthly newsletters.

PID UK is reliant on voluntary donations. To make a donation, please go to www.piduk.org/donate

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