Great Ormond Street Hospital for Children NHS Foundation Trust: Information for Families

Transient hypogammaglobulinaemia of infancy (THI)

This information sheet from Great Ormond Street Hospital explains the causes, symptoms and treatment of transient hypogammaglobulinaemia and where to get help.

Hypogammaglobulinaemia means there are low levels of immunoglobulins (also known as antibodies) in the body. These are part of the immune system which is the body's defence against infection.

Transient hypogammaglobulinaemia of infancy (THI) is a mild form of the condition that can affect young children. The immune system matures more slowly than usual, but eventually functions entirely normally. It is quite common and often does not produce any symptoms.

What causes hypogamma-globulinaemia?

The cause is not known. The rate of development of the immune system varies greatly between people. Transient hypogammaglobulinaemia is just when it develops slower than usual.

The true frequency of THI is unknown. It is possible that many children who suffer from frequent infections in the first few years of life may in fact have THI, but are simply never investigated.

There is a slightly increased risk for other children in the same family, compared with the general population, but the overall risk is still very low.

How does the immune system normally develop?

When babies are born, their immune systems are very immature.

There are three main different groups of immunoglobulin - IgG, IgA and IgM. Babies receive some IgG from their mothers by transfer across the placenta during the last few months of pregnancy, but they will be producing only small amounts of their own IgG, IgA and IgM.

During the first six months of life, the IgG which came from the mother is gradually lost. At the same time, the baby starts to make their own IgG, and more IgA and IgM.

However, as the baby doesn't make IgG as fast as it loses that which came from its mother, the total amount of IgG in the blood falls steadily. It usually reaches its lowest level at about six months of age. This is normal, and is called 'physiological hypogammaglobulinaemia'.

After this, immunoglobulin levels rise gradually throughout childhood, until adult levels are reached when children are about 14 years old.

If a baby is born very early, there will not have been time for the normal transfer

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of IgG from the mother to take place. Premature babies may therefore have earlier and more marked physiological hypogammaglobulinaemia than normal.

What happens to the immune system in THI?

Babies are sometimes slow to start producing immunoglobulins. All types of immunoglobulin may be low, or one or two may be normal. This problem doesn't usually last for very long, and levels in most children will have 'caught up' by the time they are three to four years of age.

In a few children, there may not be complete catch up until they are about 10 years old.

What are the signs and symptoms of hypogamma-globulinaemia?

Children with low immunoglobulin levels may have more frequent and prolonged infections than other children of similar ages. These are often throat and ear infections, or non-specific viruses.

A typical story is that the child is having to go to the doctor often and is being given many courses of antibiotics, particularly in the winter. Some parents report that the child is unwell again as soon as antibiotics are stopped.

However, it's important to remember that frequent infections in normal children are particularly common at times when they start to mix with other children, such as starting nursery or school. Lots of young children suffer from frequent minor infections and most have completely normal immune systems.

Children with THI are occasionally at risk of serious infections such as pneumonia or meningitis, but this is relatively unusual.

How is hypogamma-globulinaemia normally diagnosed?

A doctor might be concerned about possible hypogammaglobulinaemia if a child has prolonged, frequent or more severe infections than normal. The child may be referred to a paediatrician and possibly to an immunologist.

A blood test will be needed to measure their immunoglobulin levels. It can also check for specific antibodies which should have been produced following vaccination against certain infections such as tetanus. It is unlikely that more complicated tests will be necessary.

If the child is found to have low levels of vaccination antibodies it may be necessary to give some 'booster' immunisations, followed by a repeat blood test, to check that the child is properly protected against certain infections, and as a further test of their immune system.

How is hypogamma-globulinaemia normally treated?

There is no standard treatment for THI. Management is aimed at maintaining good day to day health and a normal life, including regular school or nursery attendance.

Some children can be managed simply by treating infections quickly as they arise.

However, if a child is getting very frequent infections - perhaps every four weeks - they may need to be given a regular low dose of antibiotics. This can be very successful, and can sometimes transform the child from being constantly unwell, feeling miserable and growing slowly, to a normal, lively, happy one.

Regular antibiotics can be continued for several years if necessary, although in practice this is unusual. In some children, regular antibiotics are only necessary during the winter months.

Occasionally children with THI may have had, or continue to have, more serious infections. In this very small group, replacement immunoglobulin may be considered. This is called immunoglobulin therapy. This might be continued for several years but would not usually be needed after about 10 years of age.

However, if infections and the degree of hypogammaglobulinaemia are severe enough to require immunoglobulin replacement there is a higher chance that the problem will persist and evolve into a condition known as 'common variable immunodeficiency ' (CVID).

This is when the condition does not improve with time and a child's immunoglobulin levels remain low or even fall further. This means a long-term immune deficiency develops, called CVID.

It is important to emphasise that most children with recurrent infections and low immunoglobulin levels in infancy will not develop lifelong problems, but will eventually have normal immune systems and lead normal healthy lives.

What happens next?

There are no long-term problems for almost all children with THI. The condition gets better by school age in the vast majority of children. They will grow and develop well and lead normal healthy lives.

Check-ups every few months will be necessary with regular blood tests every six to 12 months.

However, if the child has had a serious infection before the condition was recognised, it is possible that there could be some damage, particularly to ears and lungs.

Hearing may be affected and require follow-up by ear, nose and throat specialists, and audiologists. Lung damage is much more unusual and only occurs if there have been repeated episodes of pneumonia.

Most children will have had their first immunisations before their THI is diagnosed but any will not yet have received MMR, which is a live vaccine. Part of the initial investigation of THI includes assessment of antibody responses to vaccines. If good responses

to the first set of vaccines can be demonstrated, then there is no reason not to proceed with MMR.

If, however, the responses are poor or absent, MMR should be delayed until the immune system can be shown to be maturing - with evidence of good responses to previous vaccines. In most infants with THI there is no evidence that live vaccines should be avoided.

Children with THI should ideally lead completely normal lives. They can take part in all activities. The only difference will be that you should ask your GP early if your child is unwell, since antibiotics may be needed.

Further help and advice

Talk to the child's doctor or health visitor.

There is no support group specifically for THI, but the following organisations may be able to offer support and advice and put parents in touch with other families with experience of THI.

Contact a Family
Helpline: 080 808 3555
Website: www.cafamily.org.uk

Primary Immunodeficiency Association
Helpline: 020 7976 7640
Website: www.pia.org.uk

Notes

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