

THI

Transient hypogammaglobulinemia of infancy (THI)

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About this booklet

This booklet provides information on transient hypogammaglobulinemia of infancy (THI). It has been produced by the PID UK Medical Advisory Panel and Patient Representative Panel to help answer the questions patients and their families may have about this condition but should not replace advice from a clinical immunologist.

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Summary

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

Transient hypogammaglobulinemia of infancy (THI) is a form of the condition that can affect young children. Typically the immune system matures more slowly than usual but eventually functions entirely normally. Those affected are young children (up to school age) who have more frequent and prolonged infections than their peers because their immune system is slower to develop.

Diagnosis of THI is confirmed by a blood test that measures the immunoglobulin levels and by using blood tests to look for antibodies to previous immunisations. Most children who have low antibodies have THI and get better quite quickly, and most only need to take preventative antibiotics for a year or two. However, a small minority of children with THI may need immunoglobulin treatment that can usually be stopped at some point so that the function of their immune system can be reassessed to see if they still need this treatment. There are usually no long-term problems for almost all children with THI. The condition gets better by school age in the vast majority of children. Most children with THI will grow and develop well and lead normal, healthy lives.

How did my child get THI?

The exact causes of THI are not known. The rate at which the immune system develops varies a lot between people. THI occurs when the immune system develops slower than is usual.

Doctors do not know how many children get THI. This is because many children who suffer from frequent infections in the first few months of life may have THI but are not investigated.

The immune system and THI

When babies are born, their immune system is not yet fully formed. Doctors sometimes refer to this as babies having an 'immature immune system'.

There are three main types of immunoglobulin – IgG, IgA and IgM – that protect us from infections. Babies receive some IgG from their mothers by transfer across the placenta during the first few months of pregnancy and produce only small amounts of their own IgG, IgA and IgM. However, as the baby doesn't make new IgG in the first few months 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 hypogammaglobulinemia'. 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 of IgG from the mother to take place. Premature babies may therefore have earlier and more marked physiological hypogammaglobulinemia than normal.

The immune system in children with THI

In children with THI all types of immunoglobulin may be low, or one or two may be abnormal. This problem doesn't usually last very long, and levels in most children will have 'caught up' with their peers by the time they are three to four years of age.

In a few children, because of the way their immune system develops, there may not be complete catch up until they are about 10 years old.

Family planning and THI

There is a slightly increased risk of developing THI for other children in the same family compared with the general population, but the overall risk is still very low. Currently there are no genetic tests that can help address this level of risk in a given family, but research is ongoing in this area.

What are the symptoms of THI?

Affected children with low immunoglobulin levels may have more frequent and prolonged infections than children of similar ages. These are often throat and ear infections or a 'non-specific' viral infection, where it is not possible to say exactly what virus is causing it.

A typical story is a child having to go to the doctor often and being given many courses of antibiotics, particularly in the winter. Some parents report the child is unwell again as soon as the antibiotics are stopped. However, it's important to remember that frequent infections in children are particularly common at times when they start to mix with other children, such as at nursery or school. Lots of young children have frequent minor infections and most have completely normal immune systems, so this can make it harder for doctors to distinguish children with THI from other children.

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

Making the diagnosis

The diagnosis is confirmed by a blood test that measures the immunoglobulin levels. This blood test may be performed by a GP or a paediatrician. The test may also check for specific antibodies which should have been made following normal childhood vaccinations, e.g. the Hib vaccine against the bacterium

Haemophilus influenzae B or the Pneumococcal vaccination for *Streptococcus pneumoniae* infections. In many cases it is unlikely that more complicated tests are necessary.

If your 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 your child is properly protected against certain infections, and as a further test of their immune system.

Treatment

Treatment of THI is dependent on the severity and frequency of your child's infection. Management of THI is aimed at maintaining good day-to-day health and a normal life, including regular nursery or school attendance. Some children can be kept well simply by treating infections as they arise. However, if your child is getting very frequent infections – perhaps every four weeks – they may need to be given a regular dose of antibiotics. This can have very successful outcomes by preventing periods of illness, and can make a real difference to the quality of life your child has.

Regular antibiotics can be continued for several years if necessary, although this is unusual. Some children may only need regular antibiotics in the winter months.

Occasionally some children with THI may have had, or continue to have, more serious infections. In these rare cases your doctor may decide your child needs replacement immunoglobulin therapy. Immunoglobulin therapy contains antibodies that help fight infection. This treatment might be continued for several years but would not usually be needed after about 10 years of age.

Are there any other associated health problems with THI and how will my child's health be monitored?

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. Children will grow and develop well and lead normal, healthy lives.

Monitoring is usually by clinical review (check-ups) every few months, with regular blood tests every 6-12 months. Your clinical immunologist will be on the lookout for any complications.

If your child had a serious infection before the condition was recognised, it is possible that there could be some damage, particularly to the ears and lungs. Hearing may be affected and require follow-up by ear, nose and throat (ENT) specialists and audiologists. Lung damage is much more unusual and occurs only when there have been repeated episodes of pneumonia.

The majority of 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 lives. However in rare cases, if the condition does not improve over time and a child's immunoglobulin levels remain low or even fall further, there is a higher chance that the problem will persist and evolve into a long-term immune deficiency known as common variable immune deficiency (CVID).

Immunisation

If your child has been diagnosed with THI it is always best to seek medical advice before any more immunisations are given.

However, most children will have had their first immunisations when they were a baby and before their THI is diagnosed but may have not yet received the MMR vaccine (a live vaccine). As part of the initial investigation of THI, the antibody response to vaccines is assessed and if good responses to the first set are shown, then in most infants with THI there is no evidence that live vaccines should be avoided (including 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.

Living with THI

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

Glossary of terms

antibody - a type of protein (immunoglobulin) that is produced by certain types of white blood cells (plasma cells - a type of B-cell). The role of antibodies is to fight bacteria, viruses, toxins and other substances foreign to the body.

audiologist - a medical specialist that helps children and adults who suffer from a loss of hearing or may have problems with tinnitus or balance.

common variable immune deficiency (CVID) - a primary antibody deficiency. People with CVID have either no immunoglobulins in the blood or low levels and require immunoglobulin replacement therapy.

genetic tests - used to find out whether a person is carrying a specific genetic variation (altered gene) that causes a particular medical condition.

hypogammaglobulinemia - a condition where the blood has abnormally low levels of immunoglobulins (antibodies) that help fight infection.

immune system - the structures and processes that protect the body against infection and disease.

immunoglobulins - proteins (globulins) in the body that act as antibodies. They work to 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.

immunoglobulin replacement therapy - immunoglobulin (IG) replacement therapy is a plasma-based treatment. The immunoglobulin contains antibodies that help fight infection. This treatment can be given through a vein or through the skin.

meningitis - an infection of the meninges (protective membranes) that surround the brain and spinal cord. It can be bacterial, viral, tuberculous or inflammatory (non-infectious).

MMR vaccine - a live vaccine against measles, mumps and rubella (German measles).

pneumonia - a swelling (inflammation) of the tissue in one or both of your lungs. It is usually caused by an infection.

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 (IPOPI), 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 bulletins.

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