

Transient hypogammaglobulinaemia of infancy (THI)

What is transient hypogammaglobulinaemia of infancy?

Transient hypogammaglobulin-aemia of infancy (THI) is the name for a condition in which the immune system matures more slowly than usual, but eventually functions entirely normally.

'Hypogammaglobulinaemia' means that there are low levels of immunoglobulins (also known as antibodies) in the body, which are important in fighting infections. There are three main different groups of immunoglobulin - IgG, IgA and IgM.

How does the immune system normally develop?

When babies are born, their immune systems are very immature. They will have received some IgG from their mothers by transfer across the placenta during the last few months of pregnancy, and they will be producing only small amounts of their own 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 his or her own IgG, and more IgA and M. 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 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 ten years old.

What problems does THI cause?

Children with THI 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 their 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.

What can happen in the long term?

The problem gets better by school age in the vast majority of children. However, a small minority of those thought to have THI do not improve with time, and their immunoglobulin levels remain low or even fall further. In this very small number of children, a long-term immune deficiency develops,

known as common variable immunodeficiency (CVID). A separate information leaflet is available which describes CVID, but it is important to emphasise that most children with recurrent infections and low immunoglobulin levels in infancy will not develop lifelong problems, but will have normal immune systems and lead normal healthy lives.

What causes THI?

This is not known. The rate of development of the immune system varies greatly in different individuals, and THI probably simply represents one end of the spectrum.

How common is THI?

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.

Is there a risk that other children in the family could have THI?

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 will your child be investigated?

If there is concern that your child suffers from more frequent, more prolonged, or more severe infections than normal, he or she may be referred to a paediatrician and possibly to an immunologist. A blood test will be needed to measure his or her immunoglobulin levels and probably to check for specific antibodies which should have been produced following vaccination against certain infections such as tetanus and Hib. It is unlikely that more complicated tests will be 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 he or she is properly protected against certain infections, and as a further test of his or her immune system.

What is the treatment?

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 your child is getting very frequent infections - perhaps every four weeks - he or she may need to be given a regular low dose of antibiotics. This can be very successful, and can sometimes transform a 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 (see information leaflets on immunoglobulin therapy). This might be continued for several years but would not usually be needed after about ten years of age. 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 CVID.

Are there any long-term effects of THI?

There are no long-term problems for almost all children with THI. They will grow and develop well and lead normal healthy lives. If, however, they have had serious infections before the problem 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.

How will your child be monitored?

Your child will have regular reviews by an immunologist or general paediatrician, usually every four to six months. His or her immunoglobulin levels will be checked by a blood test every six to twelve months. If you are worried at any time between regular reviews, additional appointments can be made.

Do you need to take any special precautions to protect your child?

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.

What about immunisations?

Most children will have had their first immunisations, including live polio vaccine, before their THI is diagnosed. Many will not yet have received MMR. Part of the initial investigation of THI includes assessment of antibody responses to vaccines, as mentioned above. 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 infants with THI there is no evidence that live vaccines should be avoided.