

ENDOCRINE SYSTEM: A system of glands in the body which secrete substances called hormones into the bloodstream. Some of the endocrine glands include the thyroid, pituitary, the ovaries and the testicles.

ENZYME: A special protein which is formed in a living cell and which is an essential element for a particular chemical reaction taking place in that cell.

GOITRE: A visible swelling of the thyroid gland in front of the neck.

HORMONE: A chemical substance which is made by an endocrine gland and then secreted into the bloodstream. There are a large number of hormones which produce widespread effects on the body.

HYPOTHYROIDISM: A disease in which the thyroid gland is under-active. The term Congenital Hypothyroidism means that the underactivity of the thyroid gland is present at and before the time of birth.

JAUNDICE: A yellow colouring of the skin produced by an excessive amount of the pigment bilirubin. Bilirubin comes from the breakdown of red blood cells.

METABOLISM: The activity carried on by each cell in the body in which foodstuffs are broken down and energy produced.

NEONATE: A baby less than one month of age.

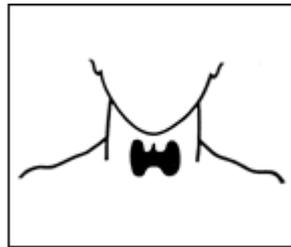
PITUITARY GLAND: An endocrine gland which is about the size of a marble and is situated at the base of the brain. This gland is very important because it controls the other endocrine glands, including the thyroid.

PRIMARY HYPOTHYROIDISM: Hypothyroidism due to disease of the thyroid gland itself.

SECONDARY HYPOTHYROIDISM:

Hypothyroidism that happens because of failure of the function of the pituitary gland.

THYROID GLAND: An endocrine gland which produces the hormone called thyroxine. The thyroid is situated in the neck, as illustrated below.



THYROID STIMULATING HORMONE (abbreviation TSH): A hormone which is produced by the pituitary gland and which stimulates the thyroid gland to secrete thyroxine. An alternative name for TSH is thyrotropin.

THYROXINE: The hormone produced by the thyroid gland. The tablets given to treat hypothyroidism contain this hormone and are called thyroxine tablets.

THE DEVELOPMENT, FUNCTION AND CONTROL OF THE THYROID GLAND

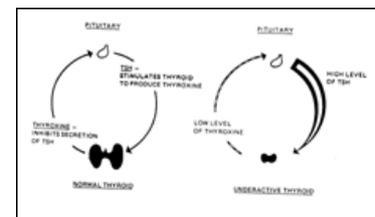
The thyroid gland begins to form very early in the developing human embryo – about three weeks after conception. It develops first in the region where the mouth and tongue will form, and then it migrates downwards into the neck to take up its final position in front and on each side of the trachea or windpipe. Very soon after it begins to develop, the thyroid gland consists of two lobes (see illustration above). The function of the thyroid gland is to manufacture thyroxine and secrete it into the bloodstream. This hormone is made in a number of steps, for each of which a particular protein called an enzyme is necessary. Thyroxine contains

the element iodine, and this is why iodine is an essential part of our diet.

The pituitary gland which is situated at the base of the brain controls the thyroid. The pituitary manufactures a hormone called thyroid stimulating hormone (TSH) or thyrotropin. When the thyroid gland is producing too little thyroxine, the pituitary is able to sense this. As a result, it increases its output of thyroid stimulating hormone which circulates in the blood to the thyroid gland and stimulates it to produce more thyroxine. If, on the other hand, the thyroid is secreting too much thyroxine, the pituitary cuts back its secretion of thyroid stimulating hormone.

Therefore, when the thyroid gland is under-active, the blood will contain a low level of the hormone, thyroxine, and a high level of the thyroid stimulating hormone.

The concepts we have just described are illustrated in the diagram below.



ACTIONS OF THYROXINE AND CONSEQUENCES OF LACK OF THYROXINE

Thyroxine is an extremely important hormone for normal growth and development. It exerts control over the body's metabolism, so that when there is not enough thyroxine, cell activity (metabolism) slows down, and when there is too much, it speeds up. Slow body metabolism may bring about the following effects:

1. Sluggishness in both physical and mental activity.
2. Low body temperature and low pulse rate.

3. Intolerance of cold weather.

4. Constipation.

These effects may be seen at all ages. In early life, there are additional consequences of lack of thyroid hormone. Babies with Congenital Hypothyroidism have the following features:

1. Slowness of Growth

While thyroxine appears not to be necessary for growth before birth, it is essential for normal growth after birth. If a baby has an untreated thyroid deficiency, he or she will remain small through infancy and childhood and end up being very short. This slowness of growth affects all parts of the body, including the skeleton.

2. Slowness of Mental Development

Intellectual retardation can occur with lack of thyroxine. The degree of retardation is dependent upon the severity of the deficiency of the thyroid hormone. When there is only a partial lack of thyroxine, little deterioration in mental function may occur. When thyroxine is completely absent and the baby receives no treatment, mental retardation may be severe. However, this will not occur if treatment is begun early. (See section on Outlook for Babies with Permanent Congenital Hypothyroidism).

3. Persistent Jaundice

As defined in the glossary, the term jaundice means that the skin has a yellow colour due to the presence of the pigment bilirubin. It is common for newborn babies to have jaundice which may last for a week or two. In untreated hypothyroidism, jaundice may persist for much longer than this.

TYPES OF CONGENITAL HYPOTHYROIDISM

We can divide patients with Congenital Primary Hypothyroidism into four groups, as follows:

1. Those with an absent thyroid gland (Athyrosis)

In this group, the thyroid gland has failed to develop before birth. The gland is absent and will never grow. Consequently no thyroxine is produced. This condition is called thyroid agenesis or athyrosis. It is more common in females compared to males – about twice as many girls as boys are affected. It occurs about once every 10,000 births and accounts for about 35% of the cases detected by Newborn Screening. The reason why the thyroid gland fails to develop in these babies is presently unknown. However, research into the condition suggests that one of a cascade of genes involved in forming the thyroid gland is not turned on at the right time.

2. Those with an ectopic thyroid gland

In these babies, the thyroid is small and poorly formed and does not occupy its normal position in the neck. It is often found at the base of the tongue, near the place where the gland first began to form in the embryo. An ectopic thyroid may have varying degrees of function. Sometimes it is very small and under-active. On other occasions, it is able to produce a nearly normal amount of thyroid hormone. Thus there is a spectrum of severity in this condition. We know that after birth an ectopic thyroid gland will not become bigger or descend to its normal position. In fact, its function will often deteriorate further with the passage of time.

Ectopic thyroid glands also occur about twice as frequently in girls as in boys. They account for about 50% of the cases detected by Newborn Screening and so are slightly more common than the cases of thyroid agenesis. Again, we do not know for sure why in some babies the thyroid gland remains in an ectopic position, but the same factors that cause thyroid agenesis may well give rise to this problem.

3. Those with a malformed thyroid gland in the normal position

This condition is sometimes called thyroid hypoplasia and it only accounts for a very small percentage of the total number of cases. In thyroid hypoplasia, the gland is small, poorly formed and occasionally consists of only one lobe.

4. Those who have a thyroid gland which has developed normally, but which cannot produce normal amount of thyroxine

This condition is known as thyroid dysmorphogenesis and it accounts for about 15% of the cases detected by Neonatal Screening. Dysmorphogenesis (enzyme defects) can be either transient, in which case it gets better with the passage of time, or else it is permanent and lasts for life. In babies affected with dysmorphogenesis, the thyroid gland is often enlarged and may be seen or felt in the front of the neck as a goitre. We will now explain in more detail its underlying causes.

Firstly let us consider permanent dysmorphogenesis. You will recall that the thyroid hormone, thyroxine, is made in a number of steps, each controlled by a particular enzyme. In very rare circumstances, one of these enzymes is missing, and this causes permanent problems making thyroxine. This abnormality is an inherited condition and therefore other babies born in to the family are at risk of having it. Usually the likelihood of another child having thyroid dysmorphogenesis due to an enzyme defect is one in four. Boys and girls are equally affected.

With transient dysmorphogenesis, the function of the thyroid returns to normal after a variable period of time. There may be a number of causes of this problem. On very rare occasions, antibodies from the mother's blood cross the placenta during the

pregnancy and decrease the function of the baby's thyroid gland. Another cause is the presence of too much iodine in the body. You may remember that we stated in a previous section that the element iodine is essential for the manufacture of thyroxine. However, too much iodine can also bring about a decrease in the function of the thyroid gland. A baby may be at risk of becoming hypothyroid if the mother takes a lot of iodine-containing medication during pregnancy and/or while breast feeding. Once, however, the excessive iodine intake stops, the thyroid gland will return to normal and the baby will not suffer any long-term ill effects.

In a few cases of thyroid dysmorphogenesis, both permanent and transient, we are unable to find out exactly the precise cause of the trouble.

NEWBORN SCREENING

All babies in Australia are screened for Congenital Hypothyroidism. This screening began in South Australia in 1977. About two days after birth, a small amount of blood is taken from the baby's heel, placed on a piece of filter paper and forwarded to a central laboratory for assay. Babies with all four categories of Congenital Hypothyroidism will be identified because they will have high levels of thyroid stimulating hormone.

Babies who have hypothyroidism as part of a pituitary gland problem will have low or undetectable levels of TSH and will NOT be identified by the Screening Program.

The reason why Newborn Screening is carried out are as follows:

1. It is very difficult to diagnose Congenital Hypothyroidism at birth, just by examining the baby. Some of the features described previously e.g. slow growth and impaired mental development are not present at

birth. They take some time, months in fact, to develop. Therefore, if Newborn Screening is not carried out, most cases of hypothyroidism will be missed at birth and treatment delayed.

2. Congenital hypothyroidism is a relatively common condition. About 8 new cases are diagnosed in South Australia each year (one in 3,500 births).

3. With early diagnosis and treatment, it can be confidently expected that even severely affected infants will develop normally both physically and mentally.

INVESTIGATION TO DETERMINE THE TYPE OF HYPOTHYROIDISM

When a baby is found to have abnormal results on screening, this information is immediately conveyed to his/her doctor or midwife. They then arrange for the baby to be seen within a short period of time either by themselves or by another specialist. At this visit, a medical history is taken from the parents and the baby is carefully examined in order to gain clues as to what type of hypothyroidism is present.

At the first visit, a blood test is done in order to confirm the results obtained by Screening.

The other investigation that is performed at this time is called a thyroid scan. For this test, the baby is given an injection of a radioactive substance called technetium which is taken up by the thyroid gland. Thus it is possible to see the position and shape of the thyroid and see if the gland is absent, ectopic or present in the normal position. There is virtually no risk associated with the use of technetium because only a low dose is used and its radioactivity goes away within hours. A thyroid scan can only be performed when the baby is not on treatment. This is why it is usually done at the first visit.

In some babies with thyroid dysmorphogenesis, more detailed investigations are

carried out after two or three years treatment in order to determine if an enzyme deficiency is present.

TREATMENT

In hypothyroidism, the thyroid gland is unable to make enough thyroxine for the body's needs, and therefore this hormone must be replaced. It is given in tablet form by mouth. The thyroxine that is present in the tablets is exactly the same as the thyroxine that is naturally present in the body. Thyroxine is now made by chemical means, previously it was extracted from the thyroid glands of animals.

Thyroxine is well absorbed from the digestive tract and readily enters the bloodstream. It does not have to be given by injection, like some other hormones, such as insulin (used for the treatment of diabetes).

All human beings require vitamins in their diet because their bodies are unable to make them. One can look upon the treatment of hypothyroidism as simply the taking of another "vitamin", which in this particular circumstance, the body is unable to manufacture.

The amount of thyroxine that is given depends upon a number of factors, including the size of the patient. Naturally, as the baby grows, a bigger dose will be needed. Once treatment has been started, blood tests are done at regular intervals in order to measure the concentration of the thyroid hormone in the blood. These tests are usually done every three months for the first three years of life, four monthly till age seven then six monthly thereafter. We aim to keep the thyroxine level in the blood about the upper limit of normal. With appropriate treatment, the stimulus to the pituitary gland to secrete large amounts of thyroid stimulating hormone will no longer be present. Therefore, the level of this hormone in the blood will be suppressed, but it may take

several months for this to occur.

If treatment is inadequate, e.g. if the dosage is too low or the tablets are not being given properly, the thyroxine concentration in the blood will be low and there will be an elevated level of the thyroid stimulating hormone. The baby or child may be drowsy or tired. Treatment for permanent hypothyroidism is life-long. If the tablets are ceased for a prolonged time, the symptoms already described will return.

FOLLOW-UP

Babies with Congenital Hypothyroidism are reviewed at regular intervals to assess their progress. Your doctor will want to make sure that the appropriate dosage of thyroxine is being prescribed and that there are no signs of under or over treatment. Usually very few problems are encountered once therapy has commenced.

In addition, with the agreement of the parents and doctor, all hypothyroid babies so far identified by screening in South Australia have taken part in a follow-up program at the Women's and Children's Hospital. After excellent outcomes from the first 22 years of Newborn Screened and treated children with Congenital Hypothyroidism, we no longer perform psychometric tests routinely.

OUTLOOK FOR BABIES WITH PERMANENT CONGENITAL HYPOTHYROIDISM

Before the Newborn Screening Program for hypothyroidism was instituted, the diagnosis was usually delayed, and as a result, some babies suffered permanent mental retardation. With early diagnosis, this can be prevented. From the follow-up studies being undertaken at the Women's and Children's Hospital and around the world, we have found that just about all babies and children whose only problem is hypothyroidism

have normal intelligence and are healthy in every respect.

It should also be appreciated that, just there is a range of levels of intelligence in the general community, so there is a range of intellectual abilities amongst the hypothyroid children. Whilst the majority of them are about average in mental skills, some are a lot below this and some above it. In addition, a small proportion of the children with hypothyroidism have other medical problems which may also have an effect on their intelligence.

QUESTIONS AND ANSWERS

Q. What will happen if my baby misses a dose of thyroxine or vomits up one of the tablets?

A. No harm is done if only one or two doses of thyroxine are missed. It is, of course, important that the tablets are administered regularly, so make sure that you obtain a repeat prescription from your doctor when your supplies are getting low.

Q. Can treatment be stopped at any stage, e.g. on reaching adult life?

A. In permanent Congenital Hypothyroidism, it is not possible to stop treatment. Thyroxine must be taken regularly throughout life, even when physical growth has ceased.

Q. Will any problems occur when my child has immunisations or has to take other medication?

A. No. Children with hypothyroidism can have the usual immunisations and take other medication without any problem.

Q. What are the side effects of thyroxine treatment?

A. Because the treatment of hypothyroidism involves replacement therapy with a natural hormone, no side

effects occur if the dosage is appropriate. If, however, too much thyroxine is given, the effects will be the same as those that occur with an overactive thyroid gland, viz., rapid pulse, loss of weight, restlessness, overactivity, etc.

Q. What are the risks of a further child in the family having hypothyroidism?

A. The risks depend on the cause. Most cases of Congenital Hypothyroidism are due to absent, ectopic or hypoplastic thyroid glands. These problems are not inherited and the risk of a subsequent child having a similar condition is very small. The likelihood of a baby being born with an absent or malformed thyroid gland in the general population is about one in 3000. This risk may be slightly higher when there is already one affected child in the family, but it is not a substantial risk. In the South Australian follow-up program, there are now over 100 families with children having either absent, ectopic or hypoplastic thyroid glands, but in only one family is there more than one affected child.

In the few cases of permanent dysmorphonogenesis due to an enzyme deficiency, the risk of having a second infant with the same problem is one in four (see section Types of Congenital Hypothyroidism). With transient dysmorphonogenesis, there is usually no risk of recurrence, unless the cause of the problem, e.g. excess iodine, is still present.

Q. When a person with hypothyroidism has children of his or her own, what risk do the children face of having the same condition?

A. There is only a low risk that the children of a congenitally hypothyroid mother or father will have the same problem. In general, this applies to all the types of Congenital Hypothyroidism. Even with permanent dysmorphonogenesis due to an enzyme deficiency,

the risk remains low, unless the affected person happens to marry someone who either has the same condition or is a carrier of it.

Q. Is a child with hypothyroidism more likely to get other diseases later in life?

A. No. With regard to the risk of contracting other disease later in life, hypothyroid children are no different from the normal population.

CONCLUSION

By reading this booklet, we hope that you have gained a better understanding of congenital hypothyroidism. Because of Newborn Screening, babies who are born with a thyroid problem today can be expected to grow up normally, just like other healthy children who possess a normal thyroid gland. We can confidently predict that your child with hypothyroidism will become a healthy adult and a productive member of the community.

The doctor looking after your child will always be available to discuss any further queries or concerns that you might have about the condition.

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