

## Hyperthyroidism - The Overactive Thyroid

The clinical names for an overactive thyroid gland are: hyperthyroidism (excess of thyroid) and thyrotoxicosis (poisoning by the thyroid). The main causes of an overactive thyroid gland are:

- Graves' Disease: an autoimmune disease where antibodies stimulate the thyroid cells to secrete excess thyroid hormone. This is the most common cause of an overactive thyroid (80%).
- Toxic multinodular goitre (Plummer's disease): this is an enlarged thyroid gland that has lumps on it that have become overactive.
- Toxic adenoma (single, benign, non-cancerous lump).
- Thyroiditis: this is an infection or inflammation of the thyroid gland, which may temporarily cause excessive amounts of thyroid hormone. The thyroid gland will be painful and tender. It may be painful to swallow.
- Over medication of thyroxine.
- Pituitary problems: Rarely, the pituitary produces too much TSH, which over-stimulates the thyroid.
- Very rarely, Cancer.

There are two groups of problems which can turn the thyroid into an overactive state. Firstly, there may be a control problem. This can originate right at the top of the chain of command.

The hypothalamus may produce more of the Thyrotrophin Release Hormone (TRH), thus causing overactivity in TSH production, and hence overactivity of the thyroid itself. For example, the cells responsible for TRH production may overwork, as in the case of a hormone producing cancer called an adenoma. Fortunately, not very common.

But there may be over stimulation of these cells from the brain itself. High levels of stress from major life events can be responsible. Young adults, especially women, may be subject to this. Or the TRH producing cells become insensitive to circulating thyroid hormone and overproduce to compensate.

More commonly, the pituitary itself may start producing more TSH. This can occur as a result of a pituitary adenoma, the growth producing the hormone in an uncontrolled fashion. There may be a genetic problem with these cells, which may escape from the proper controls and start doing their own thing. Or, they can become oversensitive to hypothalamic TRH, with the same result. Whatever the cause, the thyroid becomes over stimulated and more thyroid hormone is produced than is required.

Most causes of overproduction of thyroid hormone, however, occur in the gland itself. The receptors which respond to TSH may over-respond and react by overproduction of the thyroid hormones. This is a condition first described by a Japanese physician, Hashimoto.

Research has shown that the body itself makes antibodies to the thyroid tissue which initially may cause overproduction of thyroid hormone, but, in time, this effect may burn itself out and then the receptors become insensitive and the thyroid production starts to become affected

the other way; resulting eventually in underproduction of thyroid hormone. This problem of antibodies as a cause of illness applies not just to the thyroid, but to other organs and tissues as well.

For reasons which may not be clear, but again are sometimes the result of major traumatic life events, the thyroid producing cells simply overproduce. The thyroid may become subject to an inflammatory process – thyroiditis – which may run its course to leave the thyroid normal again, or subject perhaps, to an instability between over and under-activity.

The overactive thyroid is usually enlarged and clearly visible, a condition most often seen in young women. As a whole, women are more often affected than men, usually in the younger age groups; but it may occur at any age and in either sex.

Although most people are aware of the overactive thyroid – the swollen neck and prominent eyes, obvious signs – the condition is very much less common than the underactive thyroid.

Hyperthyroidism was first described as far back as 1835, by an Irish physician, Robert Graves; and a German physician, Karl von Basedow, hastened to write a paper about it in 1840. Hence in the UK we call it Graves' disease, and the Europeans call it Basedow's disease.

In general it is diagnosed without difficulty. Its treatment, however, is often not at all satisfactory. In making a diagnosis, the doctor goes by a clinical appraisal, which should follow an invariable course. He listens to the *symptoms*, and makes an examination to determine the *signs*; backing this up by blood tests. Following which the treatment is decided upon. Let's go through this in a little more detail.

## Symptoms

The most obvious of these is that the patient will appear nervous and anxious as a general rule, and indeed may be thought to be suffering from anxiety only. Most patients are losing weight in spite of a good appetite, although occasionally the patients may be anorexic. They complain of frequent and loose bowel action. They tend to be breathless and though often hyperactive, tired at the same time.

There is a usual complaint of feeling hot much of the time, always turning down the heating, and they become aware of palpitations, either because the heart beats too fast or the pulse has become irregular.

It is most important to tell the doctor ALL the symptoms you experience. Being "energetic" or "tired" isn't enough for the doctor to make a proper diagnosis. Use the symptom list enclosed. It is the doctor's job to put this all together and he can't do this if he doesn't know all of your symptoms.

**Eyes:** Eye problems can start months before other symptoms, and carry on for a while after treatment. The whites may appear bloodshot. They may have a gritty feeling and you may have a problem with bright sunlight. The upper lids may pull upwards giving a starey appearance. You may have trouble focussing or have double vision.

In Graves' Disease, your eyes may protrude, water a lot and the upper lids may become puffy. Bags may appear under the lower lids. The eyes might ache. Without treatment, your

sight is at risk from corneal ulceration. Smoking makes matters worse and it is advisable to give up.

**Hair:** This often becomes much thinner and appears “fly-away”, with a tendency to go grey. It may not take a perm.

**Neck:** Your throat may be tender and feel lumpy. Swallowing can be difficult. A swelling on your neck could indicate enlargement of your thyroid gland (goitre). Because weight loss is sometimes severe, it looks as though you have a goitre but do not.

**Digestive System:** Problems occur because the metabolic rate speeds up considerably. Some people feel hungry all the time and cannot understand the weight loss because they are eating more. Fat stores are burnt off first and then body tissue if the illness is not treated. Conversely, you may lose your appetite. You may also vomit. You may become very thirsty and pass a lot of urine.

**Heart:** Because the increase in thyroid hormones speed up metabolism, the heart beats faster. You might notice a “butterfly” feeling in your chest. Your heart may beat very fast in either a regular or irregular rhythm (palpitations). Sometimes your heart may beat so fast you will feel faint. You may also have low blood pressure.

**Shortness of Breath:** This is noticed after climbing stairs, carrying heavy objects or sometimes even walking. It can happen when you experience palpitations.

**Bowel:** You may need to go to the toilet more often but the stools are normally formed. The stools may be pale because extra fat is being rushed through the system. Some people have diarrhoea.

**Skin:** The skin may become thin, soft, warm, damp and may flush easily. You may also itch. Spidery veins may appear on your cheeks. Your hands may seem red and sweaty. People with Graves' Disease sometimes develop patches on their lower legs that are reddened and thickened (pretibial myxoedema), and the hair on the legs may be coarser. Patches may also appear on the foot or the big toe. You may also bruise more easily because the number of your platelets is reduced.

**Nails:** Nails appear thick and flaky. They may become loose at the nail bed, where dirt collects and the tips may rise up. The fingertips may also swell.

**Bones:** On-going overactivity of the thyroid gland over a long period may cause osteoporosis, which may produce aches and pains, especially in the back.

**Muscles:** Too much thyroid hormone can speed up the breakdown of muscle fibres quicker than they can be replaced. You may feel weakness all over your body especially in the shoulders, upper arms and thighs. Your hands may be swollen and painful too. The doctor may find that you have brisk reflexes.

**Temperature:** Metabolism increases and therefore our bodies produce excessive heat, which results in constant sweating, particularly at night which is often put down to the menopause. You may find yourself walking around in T-shirts and shorts in the middle of December, with the windows open and the central heating switched off!

**Oedema:** Your ankles may swell. You may be given a diuretic drug used for water retention.

**Mood:** Patients find themselves unable to cope with life's demands, lose their temper frequently and burst into tears for no reason. They may feel nervous, anxious and irritable, although some people feel apathetic. You may feel tired but be unable to sleep. Concentration becomes difficult. You may have racing thoughts and be very talkative. You may have mood swings. Anti-depressants are often prescribed.

**Sex:** You may have an increased libido (sex drive).

**Menstruation:** Your periods may be lighter than normal or even stop altogether. Periods may become irregular.

**Fertility:** Fertility is reduced in both men and women. If you do conceive, there is an increased risk of miscarriage.

**Tremor and Shakiness:** This generally occurs in the hands. It may be difficult to hold a cup and saucer. The tremor is obvious with outstretched hands. You may feel an inner tremor too.

**Overactive/Tiredness:** Many people have surges of energy and can't sit still for a minute. Some people are talkative, nervous and full of unnatural energy. They have to stay in bed because the huge amount of thyroid hormones has made them feel exhausted and unable to move. It's as though the body is in a crisis - and it is!

**Men:** A classic sign of hyperthyroidism in men is breast enlargement.

## Signs

The doctor will look for the following. Weight loss may well be apparent in a number of patients, but certainly not all; there may be staring eyes, the result of the fat behind the eyes swelling partly with fluid. This is called exophthalmos.

One classic sign is lid-lag, where the doctor asks the patients to look at his finger as he rapidly drops it in front of their vision. The upper lid lags behind the eye following the finger. The pulse will be rapid, sometimes irregular, and the hand will be unexpectedly warm to the touch; obvious too, will be a tremor of the hand.

The extra blood flow to the thyroid can sometimes be picked up by the doctor through his stethoscope; he can hear a rushing noise, which is called the 'thyroid bruit'.

The blood pressure will be revealing too: the upper (systolic) value will be unusually widely separated from the lower (diastolic) value. Another typical finding is pretibial myxoedema, a puffiness apparent over the bone of the lower leg.

Armed with all this information, the diagnosis should be clear. Confirmatory blood tests will show abnormally high T4 and/or T3 levels, and the presence of antibodies will suggest Graves' disease.

## Treatment

Firstly, you may not have to do very much. Mild degrees of thyroid overactivity can occur on a self-limiting basis, and may sometimes be left to run their own course, with an informed patient monitoring how they are, and seeking equally well-informed advice if things are not going right.

The first approach is an alert and informed assessment of progress, intervening only when necessary.

The second line of approach is to relieve symptoms until it is clear that the illness is either going to resolve itself in time or will require sterner measures. There are two medical weapons in most common use.

(i) Simple anxiolytics.

These are basically tranquillisers (eg Diazepam), and are acceptable, for a limited time where the degree of overactivity causes nervous tremor, worry, panic and palpitations.

(ii) Along with this or possibly instead, “beta-blockers” maybe used.

These are a group of compounds which prevent high levels of nervous activity reaching the tissues, and have a general calming effect on anxiety, nervous shaking, rapid pulse, in addition to their other therapeutic effects like reducing blood pressure, slowing down heart action (helping angina) and preventing migraines.

The one most widely used is Propranolol, either 10 or 40 mg two or three times a day, according to need. Even with extensive use there are very little either short-term or long-term side effects. Many doctors have found that a combination of an anxiolytic and a beta-blocker, in really small doses, works better than high doses of either by themselves and may control mild hyperthyroidism for extended periods of time.

When things are getting tougher, the next approach is the use of a chemical block on the production within the thyroid of thyroxine, which prevents the iodine molecules from attaching themselves normally to the thyronine molecule.

Two preparations have been in use for years: the commonest is **Carbimazole** (Neomercazole) (in multiples of 5 mg and 20 mg), this is usually given in a dose of 20-60 mg daily in two or three divided doses until the patient is euthyroid and then the dose is reduced to a maintenance dose of between 5 and 15 mg per day. When the symptoms have improved sufficiently and the levels of thyroxine have also reduced sufficiently, the dose may be further reduced or discontinued. It may be reintroduced if symptoms reappear.

The other is **Propyl-thiouracil (PTU)** (50 mg), the normal starting dose is 450 mg per day. Again, this dose is reduced depending on the response until a maintenance dose is found or the condition improves sufficiently for it to be discontinued. There are of course difficulties: they have been found to cause problems with the growth of white blood cells; suddenly and unexpectedly the immune system may be so compromised that a major or minor infection may suddenly appear.

Sometimes, of course, the patient is simply intolerant of the medication and becomes ill.

A variation of treatment is called “block and replace”. Enough antithyroid medication is given to suppress thyroid function completely and then supplemental thyroid hormone, as T4 or T3, to restore a euthyroid state. The reasoning behind this is that thyroid activity should be stopped so completely that when it restarts a year or so later, it remains at normal levels. Some people still feel tired on this regime.

When a regular daily dose is chosen, the amount of thyroid hormone production starts to fall,

and the circulation of thyroid hormone starts to decline. The trick, of course, is to ensure the dose is neither too much, nor too little, remembering that thyroid production and thyroid hormone requirement may vary quite a lot. If this isn't borne in mind, the result will be that the patient may be out of balance, either over or underactive.

Regular blood testing will be done to see if doses need to be adjusted.

This treatment may be used for an extended time – certainly a year or so – so long as the self-monitoring and the advice from an understanding doctor or healthcare practitioner, provides for virtual normality. Most commonly, the overactive state will, with ups and downs, tend to correct itself; and the patient may find in time the medication becomes unnecessary.

A life event or illness may, however, start it all over again, but the patient by now will recognise the symptoms and be able to deal with them. Another common sequel however, is that having normalised for a while, the thyroid activity may start running below normal.

The problem is that this running down may be slow and insidious; the loss of energy and well-being, the weight gain, may go more or less unnoticed; be put down to age, overwork, worry, bad eating, before it becomes obvious that all is not well. The informed patient will alert themselves to this and seek advice.

If the hyperthyroidism cannot be controlled, a final solution to the problem will be offered to the patient. This final solution is thyroid ablation; which means the thyroid is knocked out finally and forever.

Two approaches are chosen: the first is radioactive iodine. I 131, the radioactive form, is given to the patient as a drink. The radioactive iodine concentrates in the thyroid tissue and 'nukes it'. And secondly, surgery, where a proportion of thyroid tissue is removed.

The thyroid uses iodine as its main raw material and so this radioactive form concentrates in the colloid (hormone forming) tissue in the thyroid gland.

I 131 concentrates itself in the cells and its radioactivity destroys them. Depending on how much is given initially depends of course on the severity of cellular damage. The amount given is calculated by body weight and the presumed severity of the over-activity of the thyroid forming cells.

There are three possible scenarios. One is that the calculation was right. The amount of thyroid tissue left is just right to produce the right level of hormones in the bloodstream. Of course the cells may later partly recover, and then it may have to be done all over again or further damage and loss of function may occur and the thyroid as a whole may become underactive.

The second scenario is that the patient continues to have an overactive thyroid in spite of treatment, and a further dose of radioactive iodine - or doses - may have to be given at once.

The third scenario is a good deal more common. Overkill becomes evident in a few days, and thyroid hormone in the bloodstream falls pretty quickly. Very soon thyroid replacement (usually thyroxine) becomes necessary.

The second approach is thyroid surgery. Let it be said at once that growths or cysts in the thyroid must be treated by surgical removal or a drainage procedure; and a much enlarged thyroid which interferes with breathing or swallowing leaves no option.

Partial thyroidectomy to reduce the amount of thyroid hormone forming tissue is an option for some endocrinologists.

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