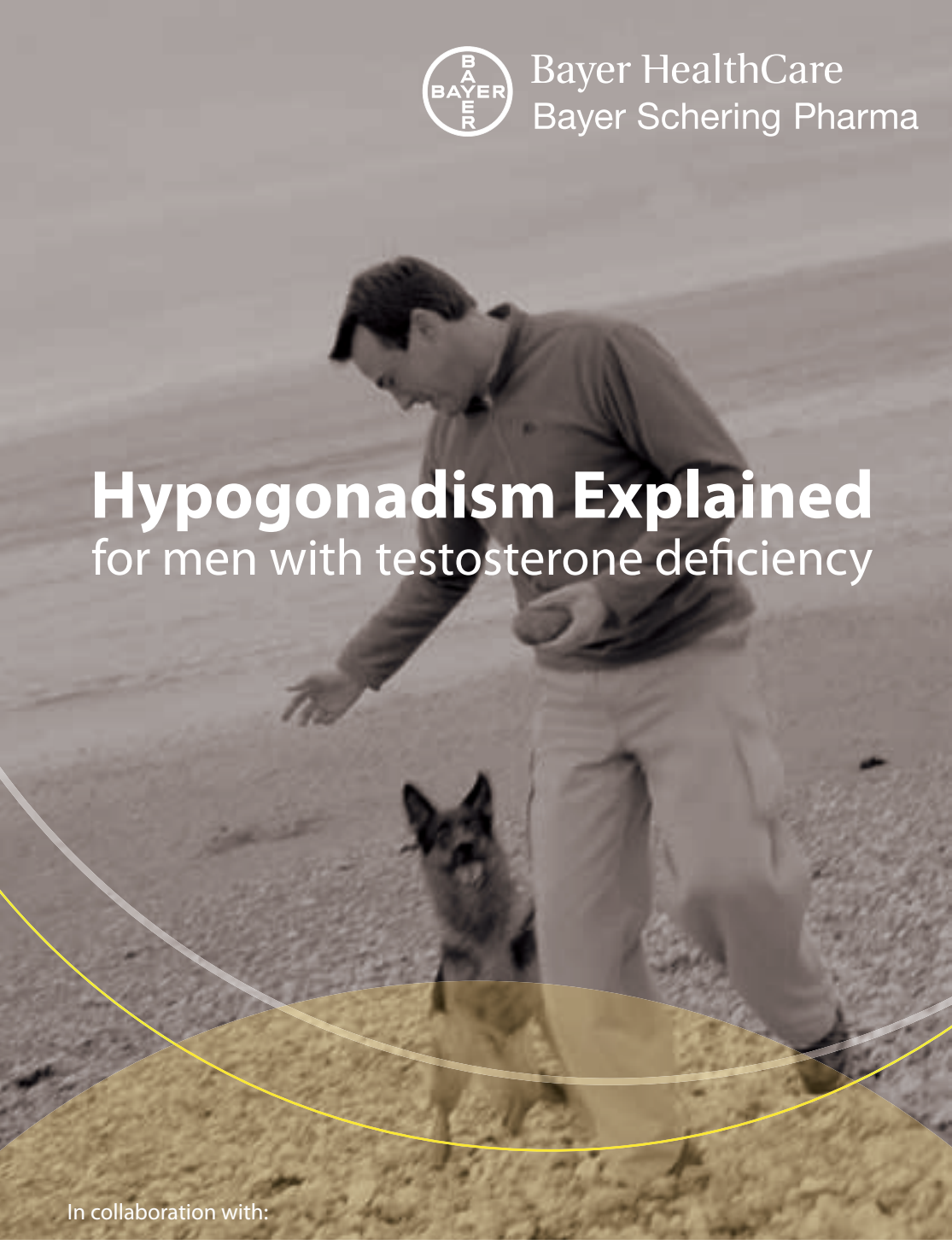
Bayer HealthCare
Bayer Schering Pharma



Hypogonadism Explained

for men with testosterone deficiency

In collaboration with:

HYPOHH

eXtra Klinefelter's Syndrome Association

The Pituitary Foundation

Introduction

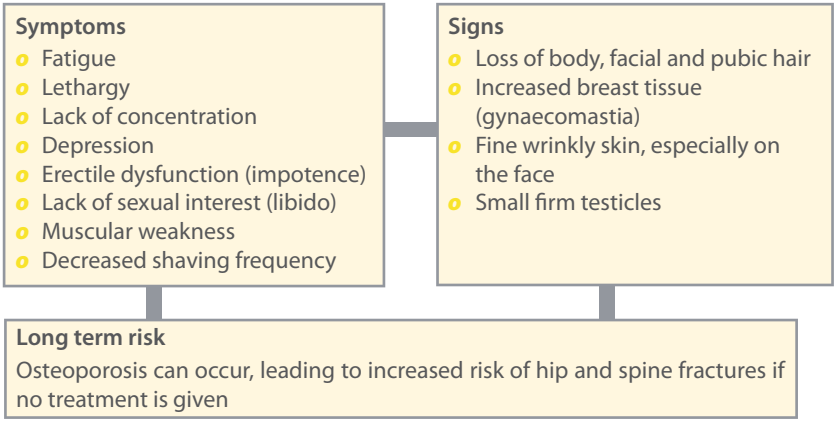
If you've just been told that you have hypogonadism or you're looking to find out the facts about hypogonadism, then this booklet is for you. Here we hope to answer most of your questions about hypogonadism: what it is, how it affects you and how it can be treated. If you have any additional or unanswered questions you can speak to your doctor or nurse, or contact one of the support groups whose details are listed on page 10.

What is hypogonadism?

Hypogonadism is the medical term for having a very low testosterone level. It is caused either when the testicles do not function normally or when internal hormone production is out of balance. Hypogonadism can affect men of any age.

So why is testosterone so important? Testosterone not only enables a man to have an erection and experience sexual desire (libido), it is also important for maintaining muscles, healthy bones, positive mood and physical energy.

Because of this, the effects of low testosterone span a whole range of symptoms such as lack of energy, depression, loss of libido, loss of facial and body hair and, potentially, increased risk of developing osteoporosis.



Symptoms of low testosterone

What causes hypogonadism?

There are two main types of hypogonadism and each has its own cause; these are referred to as primary and secondary hypogonadism. In this section we explain the basic differences between the two and list a few of the conditions linked to them. We will also look at a third kind of hypogonadism, late-onset hypogonadism, which tends to develop later in life.

Primary hypogonadism is the term used for low testosterone resulting from a problem within the testes. This may be due to a genetic cause, the most common of which is Klinefelter's syndrome, or due to physical damage to, or removal of, one or both of the testes.

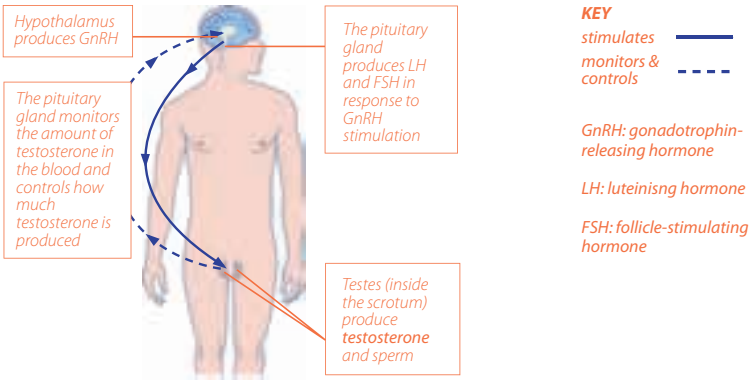
In Klinefelter's syndrome the testes develop poorly. This means that during puberty the testosterone level does not rise as it usually would in other teenage boys. Therefore muscle growth and body hair may not develop as they do in most teenagers. Additionally, the voice is unlikely to break and a man's overall appearance may be less masculine.

Illnesses such as mumps, cancer, liver or kidney disease and diabetes can also affect the testes and cause primary hypogonadism.

Secondary hypogonadism results when the complex hormonal system responsible for producing male sex hormones goes out of balance or breaks down. When the system works properly the testosterone level is kept within a normal (or 'physiological') range by the release of a system or cascade of hormones (collectively known as 'sex hormones').

These are regulated by two parts of the brain – the hypothalamus sends the first hormone which then triggers the pituitary gland to release two more hormones (luteinising hormone and follicle-stimulating hormone). These then stimulate the testes to produce testosterone and sperm.

This cascade is illustrated in the diagram overleaf.



Production of male sex hormones *(modified from The Pituitary Foundation's Hypogonadism and Infertility: A Guide for Men)*

A breakdown or imbalance at any point in the hormone cascade (above) can lead to a reduced level of testosterone.

Secondary hypogonadism can also be due to genetic causes, the most common of which is Kallmann syndrome, or other conditions such as a pituitary tumour, malnutrition or long term illnesses such as kidney failure or diabetes.

Another type of hypogonadism that we are more recently gaining a better understanding of occurs when a man's testosterone level falls below the physiological range as he gets older. Although a decline with age is natural, some men's testosterone levels may fall too low.

This is referred to as ***late-onset hypogonadism***. This is due to a mixture of reduced function of the testes and less hormonal stimulation from the brain, essentially a combination of primary and secondary causes. The onset of symptoms tends to be gradual, so may go unnoticed for some time.

Whichever type of hypogonadism you may have, the key signs and symptoms tend to be similar (see page 1), varying only by the age at which hypogonadism occurs.

How common is hypogonadism?

Although not a common condition, it is hard to say exactly how many men are affected by hypogonadism. Doctors believe that around five in every 1,000 men in the UK are living with some form of hypogonadism. So you are definitely not on your own.

The most common known cause of hypogonadism is thought to be Klinefelter's syndrome, which occurs in between one in 500 and one in 1,000 men. Kallmann syndrome is a less common condition, which affects around one in 7,500 men. Late-onset hypogonadism is often left undiagnosed, yet is estimated to affect as many as 12 in 100 men over the age of 40.

How is hypogonadism diagnosed?

A GP will usually carry out an initial assessment of your symptoms. They are likely to ask a number of questions about your sex life as well as other factors impacting on your health such as any medication you are taking, your lifestyle, your diet and whether you exercise. Your GP might also do a blood test to measure your testosterone level and if this is low, you will probably be referred to a specialist, usually an endocrinologist or urologist. They, in turn, might need to carry out a full medical assessment, physical examination, and further blood tests. If a genetic cause is suspected, this blood test will include a chromosome analysis as well as measuring your testosterone level. This will determine whether your symptoms are due to primary or secondary hypogonadism. The blood tests are usually done in the morning as this is when the testosterone in your blood is naturally at its highest.

If the specialist is unable to make a diagnosis, you might need to undergo a few more tests, which may include looking for enlargement of the pituitary gland (which regulates the testosterone level in your blood). This is usually done by an MRI (magnetic resonance imaging) or a CT (computed tomography) scan. Sometimes a bone density scan (a special scan of your hips and spine) may be recommended to check whether there is any sign of weakening of the bones (osteoporosis), which can occur when low testosterone is left untreated. Although these seem like a lot of tests to perform, these steps are very important in making an accurate diagnosis of hypogonadism and may influence the management and treatment you receive.

How can hypogonadism be treated?

The good news is that there are now many different ways to provide the testosterone you are lacking – called testosterone therapies. They are designed to bring your testosterone level back in line with the normal ('physiological') level and help you to feel better.

Testosterone therapies are available in everything from implants and injections to gels and capsules, so you're bound to find a treatment that will suit you. Here we've reviewed the different methods to give you a better idea of what's out there, so you can make an informed decision together with your healthcare professional as to which one would be best for you.

Injections

Testosterone injections are given deep into the muscle (intramuscular) and contain testosterone that has been specially modified so that it is released gradually. As with any medication, it can cause some side effects - the most commonly reported one is injection site discomfort. There are two types of injections – short-acting and long-acting.

Short-acting injections (every two to three weeks)

Short-acting injections need to be given every two to three weeks by your GP or nurse. These include Sustanon® 250 (blend of: testosterone isocaproate, testosterone decanoate, testosterone phenylpropionate), Virormone® (testosterone propionate). They don't require daily administration and last for weeks at a time. Short-acting injections have been used in the UK for 30 years, but they may be associated with mood fluctuations. Immediately after the injection, energy levels and mood tend to be significantly improved, but then, as the testosterone level tails off over time, symptoms of tiredness and irritability may return for some people.

Long-acting injection (every 10 to 14 weeks)

More recently a long-acting injection, Nebido® (testosterone undecanoate), has been made available. Six weeks after the initial injection, your GP or nurse may administer the next injection ('loading dose'). Once the testosterone level is stabilised, injections are only needed once every quarter (between 10 to 14 weeks) minimising visits to the doctor. This type of injection does have quite a large volume. However, once administered it maintains the testosterone level within the physiological range, minimising the mood fluctuations which may be seen with some short-acting injections.

Testosterone gels

There are three testosterone gels available (Testogel®, Tostran™ and Testim™), which are applied to the skin and quickly absorbed. Gels need to be applied every day around the same time as they last 24 hours, over the course of which testosterone is released steadily, mimicking the physiological level. Each gel should be applied to a specific area of the body, such as the arms or the abdomen, so be sure to read the patient information leaflet supplied with the therapy. Occasionally testosterone gel can cause skin irritation in some people.

Care should be taken to avoid skin-to-skin contact with other people as the testosterone could rub off on them. However, the gel is absorbed into the skin quite quickly and once it is absorbed clothing can be worn without affecting its release in the body. Alternatively, to minimise the chance of transfer, the application site can be washed after about six hours.

Testosterone patch

Andropatch® (testosterone) is a sticky patch, which releases testosterone slowly and may be applied to your back, stomach, upper arms or thighs. It is recommended that it is changed at about 10 o'clock each night and left on for 24 hours, so that the testosterone level mimics your natural testosterone cycle.

The majority of people may at some stage experience some redness and itching or rashes on their skin where the patch has been. These effects usually disappear within ten days of removing the patch.

Testosterone implants

Testosterone pellets are implanted under the skin in the lower abdomen or buttock. This does require minor surgery, usually under a local anaesthetic in a hospital. The pellets (usually three to six pellets are implanted at a time) dissolve gradually and last between three and six months. After this time new ones are added to maintain the testosterone level.

In some cases, implants can cause slight bleeding, scarring or infection where they've been inserted. It is also possible that the implants cause a bump (extrusion) or that they are pushed out of the body (expulsion).

Testosterone capsules

Restandol® (testosterone undecanoate) capsules are another treatment option. They're usually taken three to four times a day for the first two to three weeks. Once the testosterone level has built up, the dose is gradually reduced to one to three capsules every day.

Capsules should be swallowed whole with a fatty meal to help with absorption. However, because everyone's metabolism is different, it can be difficult to maintain the level of testosterone and the number of capsules needed may vary from individual to individual.

Are there any side effects?

Testosterone therapy is there to help you feel better. However, as with any medication, it can cause some side effects. The most common ones are skin reactions at the application site or injection site reactions. Other side effects are rare.

Occasionally, you might get slightly spotty skin (acne) when you first start treatment. This is because testosterone stimulates glands in the skin that counteract dryness and wrinkling, which can cause greasy skin. But this usually settles with time.

In rare cases, frequent or sustained painful erections can occur. In these cases, your doctor will reduce the dosage or discontinue treatment.

In rare cases, men who are obese or have chronic lung disease may experience a sudden obstruction to their airway while sleeping, interrupting their breathing (known as sleep apnoea). This usually resolves as treatment continues, but your doctor may want to review your treatment if this occurs.

In some cases, testosterone therapy has affected behaviour – possibly leading to aggression. This is more common if you have never had a physiological testosterone level.

These side effects tend to be rare so you may never experience any of these effects. If they do cause you concern discuss this with your doctor or nurse.

What tests are needed to monitor testosterone therapy?

Before you start therapy your prostate gland will need to be examined to check for prostate cancer. This is important because testosterone therapy can lead to an enlarged prostate gland. However, testosterone therapy itself is not known to cause prostate cancer. Your doctor should also make checks on your prostate regularly during treatment, generally annually. However, this may increase or decrease in frequency depending on age.

Your testosterone level and symptoms will be monitored a few weeks after you begin therapy to check that you are getting the right amount of treatment. After that they will be monitored usually every six months to a year.

Testosterone therapy can increase the number of red blood cells in your blood, which can affect circulation. When you have your regular blood tests, your red blood cell count will also be analysed. Liver function tests are also required as prolonged exposure to testosterone therapy can alter levels of some liver enzymes.

Over time you should find that your mood, sex drive and muscles are improved and growth of body hair will also show that your treatment is working. It is important not to expect rapid improvements; several months of treatment may be required before changes are apparent.

Real life stories

David, 58, tells his story:

"Before I was diagnosed with low testosterone, my two daughters used to call me a grumpy so-and-so because I'd completely lost interest in everything and everyone around me, even the grandchildren! The only thing I did do a lot was rowing – I'd row with my wife, my daughters and it was always about stupid things.

"Now that I am on a testosterone therapy, I don't think of myself as being ill or having an illness – I can just get on with life and it makes me feel like a different person. My wife and daughters have also noticed the difference.

"In some ways, I almost look forward to the treatment because I know that it's because of it that I am feeling good and able to get on with life."

Howard, 47, shares his experience:

"In May 2002 I was diagnosed with Klinefelter's syndrome at the age of 42. There are many symptoms associated with this condition and some of these can be alleviated with testosterone therapy.

"Before taking testosterone I was a very emotional person. I used to cry an awful lot, in fact way too much for a man. In my late thirties I began suffering from anxiety attacks and these became gradually worse until I was agoraphobic (afraid of open spaces). I also had low motivation, low self-esteem, low sex drive and an inability to build muscle mass.

"After taking testosterone my self-confidence has improved significantly and the crying has completely stopped. I've lost weight, my muscles are stronger and I've much more stamina. It has taken about four years to really feel the benefits of taking testosterone and the most noticeable improvement has been the lack of anxiety attacks. I feel much more in control of my life."

Additional support and information

Pituitary Foundation
PO Box 1944
Bristol BS99 2UB
Tel: 0845 450 0375
www.pituitary.org.uk

It is estimated that there are between 50,000 and 70,000 pituitary patients in the United Kingdom. To meet the need for information and support, in 1994, The Pituitary Foundation was launched, with charitable status following in September 1996. The Foundation is now a national support, information and advocacy organisation for pituitary patients, their families, friends and carers. The Foundation operates throughout the UK and Republic of Ireland.

Klinefelter's Syndrome Association
56 Little Yeldham Road
Halstead, Essex CO9 4QT
Tel: 0845 230 0047
www.ksa-uk.co.uk

Founded in 1990, the Klinefelter's Syndrome Association came into being as a support group for all those affected by Klinefelter's Syndrome, including families, friends and carers. The support is offered by way of a dedicated website, helpline, membership newsletter and annual conference. Creating an awareness and greater understanding of the condition and its implications is a further role to which the Association feels compelled to participate.

HYPOHH
12 Ingles Drive
Worcester
Worcs
WR2 5HR
kallmann-syndrome@hotmail.co.uk
www.hypohh.net

HYPOHH stands for 'Helping You to be POsitive about Hypogonadotrophic Hypogonadism'. Kallmann syndrome is a form of HH. This rare hormonal condition results in a failure to commence or to fully complete puberty. This results in a very low testosterone level in men and very often infertility in both men and women if left untreated. The HYPOHH website aims to provide information on diagnosis and treatments available in addition to providing a forum where people can talk to other people with the same condition.

This leaflet has been produced by **Bayer Schering Pharma** as an educational service to men diagnosed with testosterone deficiency.
Date of preparation: February 2009
Stock code: 9NEB29

www.hypohh.net

www.ksa-uk.co.uk

www.pituitary.org.uk