

# HORMONE REPLACEMENT THERAPY

An information sheet on some medical aspects of HRT

This advice sheet was written particularly for young women who use HRT - for example those with Turner's syndrome, who have experienced an early menopause or who had pituitary disease as a child. Everyone has a different opinion about HRT and there may be disagreement with some of the content which is offered in the spirit of informal advice. Also, as new research emerges and new preparations are released, this information will require updating.

## Introduction

Hormone replacement therapy (HRT) is a phrase which describes the replacement of oestrogen to women whose own oestrogen levels are low. The body makes many hormones and in general, when a hormone is lacking it should be replaced. For example, an under active thyroid gland is treated with thyroid hormone and diabetes is treated with insulin. The ovary makes oestrogen, progesterone and some male hormone, testosterone. Most of the debate in this area relates to the use of oestrogen.

Progesterone has a very clearly defined role. Progesterone must be given to all women receiving oestrogen who have a uterus. The reason for this is that oestrogen given on its own can cause cancer of the uterus and this is almost completely prevented when progesterone is given. Progesterone is usually given at for 12-14 days each months to bring on a menstrual withdrawal bleed.

Male hormone, testosterone, very rarely has to be replaced as it is also made by the adrenal gland. Testosterone supplements have been shown to improve sex drive in women after removal of the ovaries but none of the preparations available in the UK are perfect for use in women.

## Symptoms of oestrogen deficiency

A lack of oestrogen can cause changes in mood (depression and poor concentration), vaginal dryness and a reduction in energy, skin elasticity, and breast size. Perhaps the most common symptom of oestrogen deficiency is flushing - this can often feel like intolerance to heat. In addition to these symptoms of oestrogen deficiency, there are hidden changes which can affect health later on in life. In particular, a lack of oestrogen causes thinning of the bones, osteoporosis, and early heart disease. That is, a bone fracture or a heart attack in later life can be caused by a shortage of oestrogen.

## Benefits of hormone replacement therapy

Oestrogen treatment is very effective at reducing and often completely preventing the symptoms of oestrogen deficiency. As regards osteoporosis, oestrogen can improve the density of bone and prevent bone loss, although the extent of the strengthening of bone is very variable. On average there is a 25-50% reduction in bone fractures in women who have used HRT, compared to women who have never used HRT.

It had been thought that HRT might delay the onset of heart disease with estimates of a 30% reduction in heart attacks in HRT users. Recent reports, however, have shown that there is no benefit to the heart. These studies do show that taking HRT can reduce the risk of colon cancer and possibly Alzheimer's disease.

## Side effects of hormone replacement therapy

The side effects of oestrogen treatment include nausea, headaches, breast tenderness, a rise in blood pressure and weight gain. Usually, these side effects can be avoided by changing the type of preparation. Side effects of HRT are less with low dose preparations and with skin patch preparations.

Every woman is different - with over 50 types of HRT available in the UK it is hoped that every woman will find a suitable preparation. It is also possible to prescribe each component of HRT separately to individually tailor the mix of oestrogen, progesterone and testosterone. It may be necessary work through several types of HRT by trial and error and be prepared to make changes with time.

## Risks of hormone replacement therapy

Recently, we have learned that there is a higher risk of blood clots in women taking HRT even with natural oestrogens. Blood clots can occur in the veins of the leg - a deep vein thrombosis. HRT should not be used if a thrombosis has happened in the past. The risk of stroke is also slightly raised in women on HRT. There is no excess risk of cancer of the uterus with HRT as long as progesterone is also given. In young women whose ovarian function tends to fluctuate, there is no adverse effect on future fertility by taking low dose HRT.

Breast cancer is a common fear for women taking HRT. Several studies have suggested that breast cancer is more common in women who have taken HRT for more than ten years. There are good theoretical reasons why oestrogen might cause breast cancer. By extending the "oestrogen years" by more than ten years (that is, by taking HRT for ten years, between the ages of 50 and 60) breast cancer becomes slightly more common. Oestrogen replacement is not usually taken by women who have had breast cancer unless symptoms of a lack of oestrogen are particularly troublesome. If there is a very strong family history of breast cancer, then it is wise to have specialist advice and consider mammography. Mammograms most effective in older women and screening with mammography usually starts at the age of 45 - 50 in the UK - using HRT makes no difference to this screening policy.

## HRT and young women

It is likely that women who experience an early menopause have a *lower* than average risk of thrombosis and breast cancer. Therefore, replacing oestrogen merely returns these risks to normal - just as if the ovaries were working normally. In women who undergo the menopause before the age of 40, it may well be safe, indeed advisable, to take HRT for more than 10 years, continuing at least until the age of the average menopause at 50.

In some young women with an early menopause there is a chance of pregnancy. If a pregnancy is not wanted then the best form of HRT might be the oral contraceptive pill. Alternatively, if HRT preparations are preferred, then barrier contraception should be used. If pregnancy is wanted then low dose oestrogen replacement will not prevent a miracle pregnancy happening - indeed, most women in this situation conceive while taking HRT. There is no risk to the baby and HRT can be stopped as soon as pregnancy is discovered as the placenta makes plentiful hormones.

If the chance of pregnancy is very low then HRT is generally

better than the oral contraceptive because most forms of HRT provide oestrogen all the time instead of just for 3 weeks out of 4 with the pill. That is, symptoms of oestrogen deficiency can occur in the pill free week that is part of all combined oral contraceptives.

## NOTES ON THE VARIOUS TYPES OF HRT

This page provides a background to the types of hormones available in HRT. The trade names of preparations keep changing – a full list of these is available separately. HRT preparations can be divided into *cyclical* forms (progesterone for 2 weeks of each cycle) which cause regular periods or *continuous combined* forms (constant oestrogen and progesterone) which are designed to be 'no bleed'. Break through **bleeding with** 'no bleed' preparations is common in young women.

### • **Conjugated Equine Oestrogens**

Conjugated oestrogens have been the most widely used type of natural oestrogen because they have been around the longest. Conjugated oestrogens are extracted from the urine of pregnant mares and, although there has been some concern about the wellbeing of these animals, there is also reassurance from the pharmaceutical company that the farming conditions are satisfactory. It is treatment with these tablets that has given most of the scientific information on risks and benefits of HRT.

Conjugated oestrogens are available in two doses – 0.625 and 1.25 mg. The lower dose is roughly equivalent to *oestradiol valerate* 2 mg, *ethinyloestradiol* 20 ug or oestrogen patch 50 ug.

### • **Other 'Natural' Oestrogens**

Most other tablet forms of HRT contain *oestradiol valerate* or a similar compound and these can be extracted from soya beans but are made as synthetic copies of the natural compounds. While these preparations appear to be the same strength as conjugated oestrogen tablets, we do not yet have many years of scientific research to be certain of the risks and benefits of this treatment although they are likely to be as effective as conjugated oestrogens.

Doses of most preparations are oestradiol valerate 1 – 2 mg with one offering 4 mg.

### • **Synthetic oestrogens**

All oral contraceptive pills contain *ethinyloestradiol*, a strong synthetic oestrogen designed to prevent ovulation. Oral contraceptive pills have often been used as HRT in young women. The oral contraceptive pills, however, because they are stronger than natural oestrogens and probably carry higher risk of blood clotting (thrombosis) compared with HRT preparations. For many women with oestrogen deficiency, the oral contraceptives may be unnecessarily strong for use as HRT. Also, oral contraceptives provide oestrogen for only 3 weeks in every 4 - the fourth week being 'pill free'. For women who are oestrogen deficient, the lack of oestrogen over this pill free week can cause symptoms and it seems more natural to provide oestrogen continuously which is the case in most forms of HRT.

Oral contraceptive pills are available in four doses containing 20, 30, 35 or 50 ug of ethinyloestradiol – the top dose is not used routinely.

### • **Tibolone**

Tibolone is a synthetic hormone which has some oestrogen-like and some progesterone-like activity. This preparation is designed to prevent the symptoms of oestrogen deficiency without causing menstrual bleeding. Tibolone is effective in preventing osteoporosis but the long term effects on the risk of thrombosis, heart attacks and breast cancer are unknown.

### • **Skin Patches and Oestrogen Gels**

Skin patches are like plasters which allow oestrogen to be slowly absorbed through the skin – 'transdermal'. The patches contain oestradiol which is a synthetic copy of natural oestrogen. Some are changed every 3-4 days and others last a week. Oestrogel works in a similar way to the patch and is applied to arms, shoulders or thighs every day. The patches are helpful in reducing the side effects of the tablet forms of HRT, in particular, headache, nausea and a rise in blood pressure but have a common side effect of skin irritation. Patches are also useful for women with liver disease or raised triglyceride levels. Nasal oestrogen has recently been introduced as an alternative to transdermal oestrogen.

The dose of transdermal patches vary from 25 to 100 ug of oestradiol absorbed in each 24 hours.

### • **Oestrogen Implants**

Oestrogen implants have been very popular in previous years, when skin patches were not available. They involve a minor surgical procedure, where the implant is inserted beneath the skin of the abdomen or buttock once every six months. Implants are used less frequently now that patches are available, for two main reasons. Firstly, some women seem to "get used" to implants and find they need higher and higher doses. Secondly, if side effects occur they can last a long time and it can be difficult to remove the implant. Progesterone does not come 'ready packaged' with implants and some women do not wish to take progesterone regularly. It is very important to take progesterone regularly in order to have a period with the implant form of oestrogen in order to avoid the risk of cancer of the womb.

### • **Vaginal oestrogen**

For some women the worst symptoms of oestrogen deficiency affect the vagina – dryness and discomfort on intercourse. Oestrogen placed in the vagina can be a very effective way of relieving these symptoms. Vaginal oestrogen may be used alone or as a boost to other forms of HRT which may not be effective enough to relieve all vaginal symptoms of their own. Vaginal preparations include creams, pessaries, tablets and rings.

### • **Phyto-oestrogens**

Plant oestrogens or phyto-oestrogens are available in health shops but not by prescription. These preparations are effective in treating some of the symptoms of oestrogen deficiency and help prevent bone loss. They are however, many times weaker than prescription forms of HRT and are unlikely to be strong enough to prevent osteoporosis in young women.

## **Progesterone Treatments**

For women who have not had a hysterectomy, any oestrogen treatment must be combined with progesterone, either in tablet form or with a second patch, in order to provide a menstrual bleed. One HRT preparation uses progesterone only every three months. Alternatively, progesterone and oestrogen can be given together continuously so that no periods occur. These last two options are not recommended in young women as break through bleeding is more common in the young and the long term safety of this type of HRT has not been proven in this age group. The side effects of progesterone treatment include pre-menstrual symptoms of mood change, bloating and breast discomfort – these side effects are more prominent with the stronger progesterones – norethisterone and medroxyprogesterone and less common with dydrogesterone. All progesterone preparations used in HRT and the pills are synthetic.

'Natural' progesterone cream has been used and there is no information yet to say this is better than the synthetic products. In fact, progesterone cream can be a danger in women who have not had a hysterectomy and who take oestrogen as well. The very low dose of progesterone on the cream does not protect the uterus sufficiently.

## **Progesterone preparations used in HRT:**

- **Tablets** dydrogesterone  
levonorgestrel / norgestrel  
medroxyprogesterone  
norethisterone
- **Patches** Progesterone patches are only available as part of HRT packs
- **Vaginal progesterone**

## **Testosterone Replacement**

The ovary makes about half of the supply of testosterone - the other half comes from the adrenal gland. Some women find that lower testosterone levels reduces sex drive and energy. Testosterone replacement is available in implants or tablets (*Restandol*). Testosterone treatment can be difficult to balance because of the side effects of excess hair growth and acne - for this reason testosterone treatment is not given routinely. A testosterone precursor DHEA (dehydroandrosterone) is a useful way of providing a boost to low testosterone levels for women.

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