

HEALTHCARE ISSUES FOR WOMEN WITH TURNER'S SYNDROME

Introduction

Turner's syndrome affects about one in 2,000 females (13,000) in the United Kingdom and is caused by an abnormality of one of the X chromosomes. The normal chromosome make-up of women is to have 46 chromosomes, two of which are X chromosomes (46 XX). Men have the make-up 46 XY. Turner's syndrome occurs when one of the X-chromosomes is partly, or completely lacking (45 X). Turner's syndrome is often diagnosed at birth, when the typical physical features are noted; during early childhood, when growth can be slow, or at puberty when periods fail to start on time. When Turner's syndrome is diagnosed early, most women with Turner's syndrome first come under the care of a paediatrician but subsequent care can be very fragmented. When Turner's is diagnosed later care may be under a gynaecologist, cardiologist or endocrinologist. For many years the health issues that affect older women with Turner's syndrome have been neglected but increasingly there is seen to be a need for a dedicated health strategy for adults with Turner's syndrome. Outlined below are some of the important points in health care that particularly affect adult women with Turner's syndrome.

While women with Turner's syndrome can expect to live a long and healthy life, there are several problems which are known to be particularly common, many of which are preventable if simple health checks are undertaken. There is no up to date information on life expectancy for women with Turner's syndrome. The information which is available suggests that heart disease is more common in TS but this may reflect a past era when HRT was not used as consistently as it is today. Nevertheless, much of the health care plan for women with TS is aimed at monitoring the risk of heart disease later in life.

Being Overweight

Body weight is determined by the amount of calories taken in the diet and the amount of calories burned up. The burning up of calories is reduced in anyone of short stature and women with Turner's syndrome can find weight control quite a struggle.

Body weight needs careful monitoring in order to prevent obesity. Careful attention to diet and exercise are required to bring about weight loss. A diet sheet designed for women with TS is provided separately. Some women have reported that, because they did not excel in sport at school, exercise has not become part of their weekly routine. The best exercise plan for weight loss is sustained cardiovascular exercise such as jogging, cycling or energetic walking for one hour at a time 2 to 3 times per week. Weight gain can also occur with an under active thyroid gland and with some forms of hormone replacement therapy. Being overweight can make high blood pressure and diabetes more difficult to control.

Aortic Valve and Aorta

The aortic valve of the heart lies at the exit from the main heart chamber - the left ventricle - at the entrance to the aorta. Normally this valve has three leaflets - a tricuspid valve - and in about 10% of women with Turner's syndrome there are only two leaflets - a bicuspid valve. Usually the bicuspid valve has no ill effects but it can be a risk for infections of the heart. For this reason, it is important to identify a bicuspid valve and take preventative antibiotics for certain procedures such as dental work. An echocardiogram is the best way of viewing the aortic valve.

The aorta is the major blood vessel taking blood from the heart to the rest of the body. In about 10% of women with TS the aorta can be narrowed - coarctation of the aorta. This condition is usually

identified in childhood because of high blood pressure. Coarctation of the aorta are usually corrected surgically in childhood but it is possible that some minor forms of coarctation present in later in life. An MRI scan of the aorta is the best way of viewing the shape of the aorta but it is not clear yet how helpful routine scans of this type are.

The root of the aorta - just as it leaves the heart - can be enlarged in women with Turner's syndrome. This aortic root dilatation can occur with a bicuspid valve, with a coarctation or on its own. The size of the aortic root enlarges with age and is more likely if high blood pressure is present. Early treatment for blood pressure should be considered if a dilated aortic root is found on echocardiography or an MRI scan.

All of these heart conditions can lead to dissection of the aorta where the wall of aorta splits requiring surgical repair. Although this event is very rare, it is serious enough to require close monitoring of the heart and aggressive blood pressure treatment in some individuals.

High blood pressure

High blood pressure is a common problem in Turner's syndrome for several reasons. Firstly, kidney disease and being overweight both make high blood pressure more likely. In addition, some forms of HRT can raise the blood pressure and make weight loss difficult. Lowering blood pressure reduces the risk of heart disease, enlargement of the aorta, stroke and kidney damage. Blood pressure monitoring at least once per year and early treatment of high blood pressure is an important part of health care in Turner's syndrome. Plasma renin activity is useful screening measure for important congenital heart disease and vascular abnormalities of the kidney blood vessels which can cause high blood pressure.

Diabetes

A high sugar level in the blood is called diabetes. If diabetes is going to become a problem in Turner's syndrome, it is usually in the older age group. The risk of diabetes is greater in women who are overweight and who have a diet high in sugar. Because diabetes can exist for many years before it becomes obvious, routine checks of the urine should be undertaken, to look for mild forms of diabetes. Many of the complications of diabetes, such as eye disease, can be prevented by early detection and treatment of raised sugar levels.

Osteoporosis and Hormone Replacement Therapy

Osteoporosis is a condition where the mineral content of the bone is reduced and the bones are more likely to fracture. Osteoporosis is common in Turner's syndrome because of a lack of oestrogen and, for the most part, it is completely preventable by taking oestrogen replacements. In nearly all women with Turner's syndrome, the ovaries fail to make oestrogen and no natural menstrual periods occur. All women with Turner's syndrome who have no periods should take hormone replacement therapy (HRT). There are many forms of HRT available and it may take a lot of experimenting to find one that suits each individual. The choices vary between the oral contraceptive pill, HRT tablets and oestrogen patches. In addition to HRT, there are other measures which can help increase bone strength. In particular, keeping up a healthy amount of weight bearing exercise as outlined above and maintaining a good calcium intake in the diet. If you are someone who eats very few dairy products, then calcium and vitamin D supplements in tablet form may be advisable.

Underactive Thyroid Gland - hypothyroidism

The thyroid gland becomes under active in about 20% of women with Turner's syndrome. The risk of hypothyroidism increases gradually with age and the cause is the same as for women with out Turners - autoimmunity causing damage to the thyroid - and it is usually permanent. The risk of hypothyroidism is greater is thyroid autoantibodies are positive. An under active thyroid can cause lethargy and weight gain and a simple hormone tablet of thyroxine completely restores the body's thyroid function. Under activity of the thyroid gland can occur at any age and regular blood tests for the measurement of TSH (thyroid stimulating hormone) are required in order to detect it early. Treatment for hypothyroidism is very simple tablet treatment with thyroxine 50 - 200 ug per day.

Hearing

One of the most common problems for children with Turner's syndrome is ear infections, thankfully they do not usually continue to cause problems in adults. However, having a 'glue ear', 'grommets' and inner ear operations can all affect the hearing, making deafness in adulthood a frequent problem sometime requiring hearing aids. In addition, 'sensorineural deafness', separate from any ear, infections becomes increasingly common with age. As hearing loss can be very gradual, deafness often goes unnoticed. Formal hearing tests - an audiogram - should be available routinely at least once every five years.

Kidney Disease

Kidney disease is only slightly more common in Turner's syndrome. As mentioned above, both diabetes and high blood pressure can damage the kidneys. In addition, the kidneys can occasionally be malformed in Turner's syndrome – a horseshoe kidney, sometimes making urine and kidney infections more common. Monitoring of kidney function is a simple blood test measuring urea and creatinine. If kidney function is not perfect then early blood pressure lowering treatment may be appropriate.

Liver function

Recently, several papers have reported raised measures of liver enzymes in women with TS. Other tests of the liver such as antibodies that might affect liver function, the appearance of the liver on ultrasound and liver histology have each been consistently normal. Oestrogen replacement therapy, including the use of ethinyloestradiol, has been shown to improve liver function with lower levels of liver enzyme activity. The long term consequences of raised liver enzymes is unknown.

Fertility options from women with Turners syndrome

Fewer than 5 percent of women with TS have spontaneous, natural periods without the need for HRT. In most instances there are no eggs present in the ovaries which appear as 'streaks' of fibrous tissue. The uterus or womb is quite able to hold a pregnancy however. In this situation 'egg donation' or 'ovum donation' is the answer. This form of assisted reproduction is available in IVF clinics and involves another women donating her eggs. The donated eggs are fertilised with the sperm from the partner of a women with TS to form an embryo. When the embryo is growing well it is put in to the womb and with luck a normal pregnancy can proceed. Because women with TS have a small pelvis, delivery of the baby is usually by Caesarean section. Breast feeding can be successful from women with TS.

Because a pregnancy can be a strain on the heart, particularly if some of the heart conditions described above are present, it is vital that a check up from a specialist aware of the details of Turner's take place before fertility treatment starts.

Management strategies for adults with TS

In developing a preventative health programme for adults with TS it should be emphasised that most of the benefit is likely to come from simple measures such a weight, blood pressure, thyroid function and an echocardiogram. The place of more costly scanning of various organs is not well established, It must be remembered that only one third of women with TS carry the burden of excess morbidity – improving their prospects must be balanced against creating a 'worried well' from the remaining two thirds. One of the next challenges will be to stratify risk groups so that adult care can be tailored to the individual.

The agenda on transfer to an adult clinic is two fold. First, it is an opportunity to review the objectives of the clinic role – for many it takes the shape of an occasional 'well woman' service with HRT advice – for others it will be the coordination of several specialists providing comprehensive support. The exact make up of a multidisciplinary service depends on local expertise but might include and endocrinologist, cardiologist, psychologist, audiologist, ENT surgeon, nephrologist and gynaecologist. Beyond the medical presence, much of the pastoral care can be better provided by Clinical Nurse Specialists and Turner Syndrome Support Group representatives whose input is vital.

Early in adult care an assessment of an individuals risk profile should be assembled particularly with respect to cardiac and renal imaging the results of which are often not passed on from paediatric clinics. A suggested schedule of assessment is presented below.

Schedule for the management of Adults with Turner's Syndrome	
First visit	Height, weight, blood pressure Urinalysis U&E, LFT, γ GT, Thyroid function, Thyroid antibodies Fasting Glucose, Lipid profile, Plasma Renin activity Karyotype Bone mineral density Echocardiogram Audiogram
First visit supplementary	Renal Ultrasound Pelvic Ultrasound 24 hr ambulatory blood pressure MRI aorta
Annual Follow up	Weight, blood pressure Urinalysis U&E, LFT, γ GT, Thyroid function Fasting Glucose, Lipid profile
3 – 5 yearly	Thyroid antibodies Bone mineral density Echocardiogram Audiogram

