Hormones and Me

Turner Syndrome

Australasian Paediatric Endocrine Group

Connections for Growth

Turner Syndrome

Table of Contents

About this Book

This booklet, *Turner Syndrome*, aims to provide a basic introduction to a genetic condition which affects some girls, as well as to the features of this condition that may be seen throughout childhood and adulthood. This booklet also discusses the treatments available for some of the problems occurring with this condition.

We encourage you to discuss any additional questions or areas of concern with your doctor after reading this booklet.

Merck Serono Australia is proud to bring you this booklet from the *Hormones and Me* educational series. We hope that you find it a valuable and helpful resource.

This booklet was revised in 2012 with the help of A/Prof Margaret Zacharin (Royal Children's Hospital, VIC, Australia), a Paediatric Endocrinologist specialising in childhood endocrine disorders and a member of the Australian Paediatric Endocrinology Group (APEG).

Paediatric endocrinologists, A/Prof Margaret Zacharin and Dr Ann Maguire (The Children's Hospital at Westmead, NSW, Australia) have reviewed the *Hormones and Me* series on behalf of the Australasian Paediatric Endocrine Group (APEG).

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Introduction

The lack of, or abnormality of, the second X chromosome produces Turner Syndrome. It affects only females. They are likely to be short and lack ovaries that function correctly. There are other physical features that are common to the condition, but rarely do all occur together in one child.

This booklet is written for girls and women with Turner Syndrome and their family and friends, who wish to know more about the condition.

Much of the medical management of Turner Syndrome in childhood is to do with improving growth and final height. There may however, also be significant problems with particular aspects of care, such as the heart, blood pressure, hearing difficulties and other areas, which will be discussed in this booklet.

Hopefully, this booklet will help readers gain sufficient knowledge to enable them to understand how to help girls with Turner Syndrome with any difficulties that may arise. Some of what you read may not be relevant as it is rare for all the possible features of the condition to occur together in one child. It is necessary to discuss the details of the child's management with a specialist, as every girl with Turner Syndrome may have different and individual health problems.

What is Turner Syndrome?

Turner Syndrome affects approximately 1 in 2,500 live female births. It is a chromosomal condition and was first fully described by an American, Dr Henry Turner in 1938. Turner Syndrome is usually characterised by short stature and non-functioning ovaries which cause the absence of sexual development and infertility. Despite the poor or absent ovarian function, other sexual and reproductive organs (uterus and vagina) are normal.

The physical features associated with Turner Syndrome may include webbing of the neck (extra folds of the skin); unusually shaped nails; puffy hands and feet; coarctation of the aorta (constriction or narrowing of the main artery from the heart which can be corrected with surgery) or other abnormalities of the heart, including its valves. Feeding problems may occur in the early childhood years and as with any child, there can be learning or behavioural difficulties, which may need professional help.

"Turner Syndrome affects approximately 1 in 2,500 live female births."

For a full list of associated features please refer to the section titled 'Features of Turner Syndrome' on page 29.

It must be emphasised that some girls may have only one or two mild features of the syndrome while others may have several that are easily recognised.

The chromosomal abnormality leading to Turner Syndrome is an accident which, unfortunately, cannot be prevented. The cause of the missing or damaged chromosome in Turner Syndrome is not known and no risk

factors, e.g. mother's or father's age, diet during pregnancy, etc. have been identified. There is also no known increased risk of recurrence in any future pregnancy beyond that seen in the general population, i.e. 1 in 2,500 live female births.

The equivalent of Turner Syndrome in boys (45OY) does not occur as survival following the loss of the only X chromosome is not possible in males.

How is Turner Syndrome Diagnosed?

Although the diagnosis is initially based on the characteristic physical signs, it must be confirmed by genetic analysis. Modern methods of genetic analysis usually use a micro-array to detect abnormalities. This is not sufficient for Turner Syndrome where a formal karyotype (chromosome analysis) is required to be sure there is no abnormality of a sex chromosome. Normally, each cell has 23 pairs of chromosomes, making a total of 46 chromosomes. One of these pairs, the sex chromosomes, determines the gender of the foetus; i.e. Will the baby by a boy or a girl? In a boy the sex chromosomes will be an X and Y (46XY) whereas in girls there are two X chromosomes (46XX). In Turner Syndrome there may be a completely or partly missing X chromosome in some or all cells of the body, making 45 chromosomes (45XO, the O representing the missing chromosome). The missing X has been lost sometime during cell division from either the mother's egg or the father's sperm.

"Each individual child requires her own personal assessment and advice about her management and treatment."

There are also a number of abnormalities of the second X chromosome that can produce Turner Syndrome. In some girls with Turner Syndrome, only a proportion of their cells have this abnormality. This is known as a 'mosaic' form of Turner Syndrome and may be associated with fewer of the physical features.

Each individual child requires her own personal assessment and advice about her management and treatment. Although it is very important that the karyotype is performed, knowing the variations of karyotype usually does not alter treatment. In a small proportion (about 1%) of girls with Turner Syndrome, a particle of a Y chromosome is sometimes found. This tiny fragment causes a significant increase in the risk of an affected girl developing a tumour of her ovary. If a particle of a Y chromosome is identified, the ovaries should be removed. In the rare situation, when a girl has both the mosaic form of Turner Syndrome and a Y particle, it is also important to make sure that the uterus and vagina are normal.

When is Turner Syndrome Diagnosed?

Diagnosis is possible at birth, or even before the baby is born. Sometimes, there are features of Turner Syndrome, such as extra neck skinfolds that can be identified by ultrasound scans during pregnancy. The diagnosis is then confirmed by removing and testing some of the fluid that surrounds the foetus in a process called amniocenteses or part of the early placenta in a process called chorionic villus sampling. These tests allow examination of the chromosomes of the foetus in the womb.

Often, a girl with Turner Syndrome is not diagnosed until early childhood when growth progressively slows down.

Diagnosis may be even later, when puberty fails to occur or slows and stops during teenage years.

Any girl who is significantly smaller than other girls of her age should have a chromosome assessment done, as the condition is relatively common.

Problems During Infancy, Childhood and Adolescence

Problems in Infancy

Baby girls with Turner Syndrome may have puffy hands and feet when they are born. This is probably due to poor development of part of the lymphatic system in these areas, which drains away body fluids through small vessels under the skin. This puffiness usually disappears soon after birth, although in some girls it can remain or recur at the time of puberty. Infant girls with Turner Syndrome may have pronounced skinfolds of the neck which generally disappear, but in some cases the neck is broad with more permanent skinfolds. This is referred to as webbing of the neck. Small spoon-shaped nails may be noticeable at birth. Some girls with Turner Syndrome may be born with a heart defect caused by narrowing of the main artery leaving the heart (coarctation of the aorta). This usually requires surgery to correct the defect and allow future normal heart function.

Infancy can be a very difficult time for parents and many will find it easier to cope if the diagnosis has been made early. Anticipated problems can then be discussed openly with plans made for how to deal with them if and when they arise.

There may be difficulties with sleeping patterns. Sometimes, parents of a child with Turner Syndrome report that their child seems to need very short periods of sleep and can be over active when awake.

Problems may arise with some babies because of poor sucking and, later, difficulties with chewing and swallowing. For some babies, poor sucking is due to high arched palate and a Rosti feeding bottle may be of help. This bottle is used for infants with a cleft palate and can be squeezed so

that the milk is directed to the back of the throat, allowing more efficient swallowing without too much sucking effort.

Spoons for feeding need to be small and cups with a thick rim are helpful because they are easier to grip with the lips. A speech therapist can be of great support with feeding problems. Early feeding problems are very common but do improve and do not lead to any serious disorders. Knowing this may help parents who can be understandably worried.

Problems in Childhood

Hearing & Vision

The Eustachian tube, which joins the back of the throat and the middle ear, allowing drainage from the ears, does not work properly in many girls with Turner Syndrome. Middle-ear infections are common and hearing can be impaired. As the girls progress to pre-school age, recurrent ear infections may become troublesome and some may require grommets, which are small tubes inserted into the eardrum to drain fluid away from the middle-ear. Hearing tests need to be done regularly to check for any hearing loss.

Eyes need to be tested for short-sightedness, squints and ptosis (drooping eyelids). A squint or ptosis in one eye will require specialist care to ensure the development of normal vision in the affected eye.

Growth

Short stature is the most common feature in Turner Syndrome. Girls with Turner Syndrome are often small at birth but most retain a normal growth rate until any time for 3–7 years, when growth slows and the difference compared to friends becomes more obvious.

The average height of a woman with untreated Turner Syndrome is around 147cm, but this also depends on the height of her parents. An affected girl with tall parents is likely to be taller than an affected girl with short parents. The cause of poor growth in Turner Syndrome is due to several factors including poor growth in the womb, the absence of the growth spurt at puberty in the untreated girl and possible skeletal abnormalities. Girls with Turner Syndrome usually have normal levels of growth hormone.

"Short stature is the most common feature in Turner Syndrome."

Treatment with growth hormone to improve growth and height is usually given in childhood. The final height can be increased by approximately 5-7cm with the use of growth hormone. Final height outcome, however, is partly determined by other factors, such as parental height and age at which growth hormone and/or oestrogen treatment was started. For more information please see the section on 'Medical Management in Childhood and Adolescence' on page 15.

Behaviour

Some parents have noticed that their daughters have shown difficulties in understanding instructions or 'just don't hear' and so hearing checks are always necessary. If hearing problems are excluded, try to rephrase instructions and be specific. Instructions often need to be carefully structured so that the task and outcome is understood.

Co-ordination

Some girls with Turner Syndrome have difficulties with activities involving dexterity and co-ordination such as catching a ball. Practice and patience can improve this as a girl gets older.

Schooling & Development

Intelligence in girls with Turner Syndrome falls across the normal range and there is no increase of intellectual disability. Progress at school is generally good and there are many girls who excel, although some do have specific learning difficulties. Reading age is often advanced, whereas writing age is sometimes delayed. Difficulties experienced with spatial skills in some girls may result in particular difficulties with mathematics and geometry.

Any concerns about the development at school of a girl with Turner Syndrome should be discussed with her teacher to see where help and support are needed.

Problems During Adolescence

The adolescent years can be a difficult time when there are changes to almost all aspects of a young person's life; academic demands increase, social relationships become more complex and independence to some may seem daunting. Apart from maybe being smaller than their friends, other emotional problems may arise. Although many girls with Turner Syndrome do overcome any learning difficulties with diligence, their social skills are not always well developed and friendships do not come easily, even in comparison with other short girls. Girls with Turner Syndrome often find it difficult to be assertive. A teenager must be encouraged and supported to develop a sense of achievement and confidence in order to equip her to cope with the larger world outside her family.

Sexual Development

Apart from short stature the other main characteristic of Turner Syndrome is the failure of ovaries to function properly and therefore the failure of sexual development in these girls.

Normally, the ovaries perform two functions; storage of eggs and production of the female sex hormones – oestrogen and progesterone. Oestrogen is the hormone required for feminising a girl at puberty and maintaining feminisation throughout life. It is also necessary to build and maintain bone strength and to create a healthy profile of cholesterol and other fats in the blood.

In girls with Turner Syndrome, the number of eggs in the ovaries gradually diminishes during childhood and the ovaries usually stop functioning properly well before the age that puberty would normally begin. Without replacement oestrogen therapy, puberty will either not occur or may start with a small amount of breast development, but then just stops.

At the appropriate age for starting puberty, treatment with oestrogen will initiate breast development and later, with a treatment combination of oestrogen and progestogen, regular withdrawal bleeds or 'periods' occur. For more information please see the section on 'Medical Management in Childhood and Adolescence' on page 15.

30–40% of girls with Turner Syndrome enter puberty spontaneously, 4% achieve menarche (onset of periods) and 1% are spontaneously fertile. In those women with Turner Syndrome who do start periods spontaneously, the ovaries are likely to stop functioning in early adult life.

Infertility

Infertility is a common problem in women with Turner Syndrome due to the non-functioning ovaries. This is discussed under 'Medical Management in Adulthood' on page 20.

Medical Management in Childhood and Adolescence

The two features of Turner Syndrome in girls that may benefit from the use of growth hormone are short stature and lack of sexual development, i.e. failure to reach puberty or to progress satisfactorily through puberty.

Treatments Available to Increase Growth Rate and Final Height

Since the mid 1980's, growth hormone, oestrogen and oxandrolone (an anabolic steroid) have been given to girls with Turner Syndrome to improve growth. Oxandrolone has been used infrequently in recent years and most girls do not use this treatment now. The specialist will discuss the child's individual needs and the best treatment approach. Growth hormone treatment will continue until an adequate final height has been reached or the growing ends of the long bones have fused, meaning that maximum height has been reached.

Growth hormone is the main treatment for girls with Turner Syndrome, to increase the rate of the growth and final height. Even though their levels of growth hormone are normal, additional doses of growth hormone are needed to improve both the rate of growth and final height. Although it is known that treatment with growth hormone does improve final height, probably as much as 7cm, it is not possible to accurately predict the final height of each individual girl.

Growth hormone is given as a daily injection under the skin (subcutaneous). Help on how to give these injections and the types of injections systems available can be obtained from the girl's specialist or nurse.

Growth hormone has been used as a growth promoting agent since the late 1950's. The original growth hormone was derived from humans but was later found to have a possible viral particle contaminant which could be transmitted into those receiving the drug. This problem does not occur with the 'newer' biosynthetic growth hormone products that are manufactured using gene technology. Over 50 years experience with growth hormone treatment has not revealed any other serious side-effects, however any concerns should be discussed with the child's doctor.

Treatments Available to Initiate Puberty

When there is no ovarian function, puberty will only occur if replacement oestrogen therapy is given. Treatment with the female sex hormone, oestrogen, is given to initiate puberty in girls with Turner Syndrome. Treatment should start at a time appropriate for the individual, i.e. it may be necessary to delay puberty for 1–2 years to achieve extra height using growth hormone. However, it is now generally accepted that commencement of oestrogen should not be delayed beyond 13.5 years where possible as there is no advantage to very late use of oestrogen and height is not increased by such delay. It is important that the onset of hormone treatment is discussed with the child's specialist. The administration of oestrogen will produce all the female sexual characteristics, such as breast development, change in body shape, maintenance of pubic hair and the associated psychological changes of puberty.

"Treatment with the female sex hormone, oestrogen, is given to initiate puberty in girls with Turner Syndrome".

A starting dose of natural oestrogen is usually around 0.5 mg every second day, gradually increasing to an adult dose of 2mg per day. Ethinyloestradiol should not be used in Turner Syndrome as it increases the risk of high blood pressure. The dose is gradually increased during pubertal development. For the first year or two, only oestrogen treatment is given (that is, oestrogen not combined with another hormone, progestogen). After the dose of oestrogen has been built up to a level sufficient for the first period to occur, or the first period has occurred (this may be seen as a spotting of blood), progestogen is added. This can be given monthly, or every second or third month but 12–14 days of progestogen is necessary for adequate removal of the womb lining (as a period).

Usually the dose of oestrogen is increased to adult replacement levels over 2½–3 years. At that time it can be made more simple by the use of a pre-packaged oestrogen and progestogen preparation which delivers oestrogen every day with cycles of progestogen to ensure that a period occurs regularly. It is important to have a withdrawal bleed in order to shed the lining of the uterus (womb) and so keep the uterus healthy. The long term replacement with a 'natural' oestrogen without an 'ethinyl' component (found in the contraceptive pill) is preferable, as it greatly lowers the risk of high blood pressure and has the added benefit of providing oestrogen at all times (the oral contraceptive has 7 days of 'no hormone' each month, to allow a withdrawal bleed. Girls and women who have no ovarian function can feel very tired and miserable during this time if a standard 'pill' is used for replacement treatment).

It is important to realise that there are a number of variations in how the tablets (pills) are presented but they produce the same effect. Transdermal oestrogen (using skin patches or gel), rather than oral

oestrogen tablets, can also be used to induce puberty in girls with Turner Syndrome. If patches are used they will need to be cut into smaller pieces to achieve the lower doses of oestrogen required for pubertal induction. The specialist will discuss and help choose the one most suitable.

Apart from sexual development, oestrogen is essential for a young woman as nearly 50% of a girl's bone mass and mineral strength is built for life during puberty. If oestrogen is stopped, osteoporosis will occur, the skin and muscle age quickly and early heart disease risk is increased. Oestrogen is also important for building psychological good health and confidence. It causes brain maturation in teenage girls and is very important in the social development of a young woman.

It is now recognised that changes occur in the walls of the aorta, the large blood vessel leaving the heart to supply the body, in girls with Turner Syndrome. This area can stretch as time passess and occasionally can split. This is potentially very dangerous. These days, MRI is considered to be the gold standard for assessment for this problem even if previous cardiac echo tests have been normal. The first MRI is usually performed around age 10 years and repeated every 5 years.

NOTE: A number of girls do have spontaneous development of pubic hair, but this is caused by a hormone secreted from the adrenal glands and is not a sign that the girl has normally functioning ovaries.

Turner Syndrome in Adulthood

During childhood, girls with Turner Syndrome are usually under the care of a paediatric endocrinologist (a specialist in disorders of hormone secretion and growth in children). At the age of about 16–18 years, girls with Turner Syndrome are usually transferred to a physician who cares for adults. It is important that the adult physician is someone who is knowledgeable about Turner Syndrome, especially with regard to oestrogen replacement and fertility, as well as the other associated medical conditions.

It is extremely important to emphasise to the adolescent that there are many aspects of the medical care of a woman with Turner Syndrome that may need attention and it is very important that they do not 'drop out' from medical care. This is particularly important because of the change of emphasis from growth, which predominates during childhood, to oestrogen replacement and to maintenance of bone strength and management of fertility problems, which are the important medical features of adult life.

Medical Management in Adulthood

Hormone Replacement therapy (HRT)

Oestrogen medication is usually given as tablets in the early teenage years to commence the development of puberty. However, unopposed oestrogen (oestrogen on its own without a progestogen) is an unsafe treatment once periods have started. Treatment with oestrogen alone will stimulate the build up of the lining of the uterus and this lining will not be shed in a normal way without the introduction of progestogen. This monthly bleed is stimulated by the progestogen treatment and is necessary to keep the uterus healthy. Without progestogen, after a long time, cancerous changes of the uterus may develop. This risk is stopped when regular progestogen is used. It must be remembered that this monthly bleeding is dependant on oestrogen and progestogen therapy and is not associated with being fertile as the ovaries are not producing eggs.

Sometimes there are advantages in giving oestrogen to adult women by a route that is not via the mouth. If oestrogen is given either through a patch on the skin, a gel rubbed on the skin daily or by a small implant (insertion of a small pellet just under the skin from which the oestrogen is released slowly) it may have less effect on blood pressure and perhaps blood clotting. Non oral oestrogens/progestogens are therefore worth considering in women who have high blood pressure, migraine or a history of having had a clot or thrombosis during oral oestrogen therapy. The specialist will discuss which type is the most appropriate.

It is important that treatment with oestrogen and progestogen (HRT) is continued at least until menopausal age. This is for maintenance of general good health, mood and energy, maintenance of skin and muscle quality and normal cholesterol, as well as normal sexual function and most importantly, for prevention of osteoporosis and reducing the risk of coronary artery disease.

In older post menopausal women who have hormone replacement therapy (HRT – oestrogen and progestogen) one of the common reasons for not continuing treatment is because of the inconvenience of periods and because of the minor side-effects which may occur during the progestogen treatment phase which are similar to premenstrual syndrome. This could also apply for woman with Turner Syndrome. One way to help with this is to have continuous combined low dose oestrogen and low dose progestogen therapy which allows enough oestrogen to be given to protect the bones without causing a build-up of the lining of the uterus. The decision about which type of treatment would be the most suitable needs to be discussed with the specialist. Often in younger women with Turner Syndrome, this type of treatment results in unpredictable vaginal bleeding and it may therefore be preferable to use intermittent progestogen cycles so that periods are predictable.

Any concerns about HRT should be discussed with the doctor.

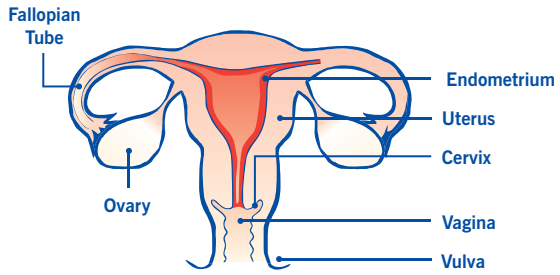
Infertility

Due to the non-functioning ovaries, very few women with Turner Syndrome are able to have children without medical help despite having regular 'periods' from cyclical oestrogen/progestogen therapy.

"Successful IVF/GIFT pregnancies have now been reported in many women with Turner Syndrome"

However, as women with Turner Syndrome do have a normal uterus it is possible to have a child through egg donation and fertility treatment. An egg can be donated from another woman and fertilised with their partner's sperm. This can take place during the technique of *in-vitro*

THE FEMALE REPRODUCTIVE SYSTEM



fertilisation (IVF) whereby the egg and sperm are put together in a test tube and fertilised.

Another method of assisted conception is Gamete Intra-Fallopian Transfer (GIFT). In this technique, the egg and sperm sample are transferred into one of the fallopian tubes to allow fertilisation to take place naturally within the fallopian tube.

Successful IVF/GIFT pregnancies have now been reported in many women with Turner Syndrome. During pregnancy the placenta will produce oestrogen and therefore additional hormone treatment will not be required during the pregnancy, after the placenta is established.

The waiting lists for such treatment can be long and it is therefore important to discuss plans for assisted fertility with the specialist as early as possible. The success rate is similar to that for other infertile couples. The major problems reported relate to miscarriage due to the (often) small

size of the uterus (womb). As lifetime oestrogen treatment regimes and IVF techniques improve, some of these problems may be overcome.

A few women with Turner Syndrome (less than 1%) have egg-producing menstrual cycles and are potentially fertile. However, it should be remembered that if a pregnancy is decided upon in women with Turner Syndrome who use their own eggs, the chances of having a baby with either Turner Syndrome or a major heart defect are extremely high. Attempts to salvage eggs from a girl with Turner Syndrome are sometimes requested. As the eggs would be unfertilised in an adolescent girl undergoing such a procedure, the current chance of success is very low. At the time of writing this, in 2012, it is thought that such procedures remain experimental.

Blood Pressure

Women with Turner Syndrome are at risk of developing hypertension (high blood pressure). Blood pressure should be measured regularly, particular during oestrogen therapy. There are several reasons why blood pressure in Turner Syndrome may rise including the possibility of a coarctation of the aorta (constriction in the large blood vessel leaving the heart), as well as problems with the kidneys or in the blood vessels within the kidney. High blood pressure can result from the use of 'ethinyl' oestradiol as found in the oral contraceptive pill. If this occurs, medication should be changed to a non ethinyl containing oestrogen. This change should significantly lower blood pressure, but it may be necessary to additionally treat the high blood pressure. However, it is very important that a woman with Turner Syndrome receive adequate oestrogen for all the reasons we have mentioned above, so oestrogen should be continued even if blood pressure needs special management.

In women who have had a coarctation, it is important to measure blood pressure in the right arm, as measurement of blood pressure in the left arm may be misleading. High blood pressure will probably require further investigations, which the specialist will discuss.

"Women with Turner Syndrome are at risk of developing hypertension."

Approximately 30–40% of girls with Turner Syndrome have some type of heart problem, most commonly a bicuspid aortic valve. For some of these problems, antibiotics may need to be given when any dental procedure or surgery occurs, to prevent bacteria landing on the abnormal valve. The specialist will advise when this care is needed.

Heart Problems

The base of the aorta where it leaves the heart can widen with increasing age and may 'split'. For this reason MRI should be used to assess the heart and great vessels in Turner Syndrome. This test should be performed around age 10 unless specifically done earlier if there is a heart disorder. It should then be repeated every 5 years.

Because many women who have Turner Syndrome are now able to consider a possible pregnancy using a donor ovum, MRI is essential before considering that option. Dissection or splitting of the aorta is a possible risk in the later part of a pregnancy. Careful heart monitoring is mandatory during pregnancy.

Osteoporosis

Osteoporosis is characterised by reduction in the amount of bone thickness and hence the development of thin, brittle bones and an increase in bone fractures. It is a major cause of pain and disability in elderly women. It is now known that the main bones mass, and thereby strength of the bones, is made during adolescence through the action of the sex hormones (oestrogen and progestogen).

Thus, any condition in which the ovaries do not produce enough oestrogens, as occurs in Turner Syndrome, makes the development of osteoporosis more likely. In addition, in Turner Syndrome it has been reported that bones may possibly be more likely to develop osteoporosis as part of the underlying condition. A good calcium intake, maintenance of normal Vitamin D levels together with regular use of HRT vastly decreases the long term risk of osteoporosis. It is important that women with Turner Syndrome continue with oestrogen/progestogen treatment throughout life until the expected age of menopause. HRT may be continued for longer, as with other menopausal woman. Risks versus benefits will need to be discussed with the specialist.

In order to prevent osteoporosis developing, women with Turner Syndrome should be screened to measure their bone density in their early twenties in order to have an accurate baseline measurement for further measurements in later life. Screening for osteoporosis and monitoring the condition of the bones, are best done using bone densitometry. Provided that the bone density measurements are adjusted for body size (and size of vertebrae), measurement is accurate. Computerised tomography

is sometimes used, as well as specialised ultrasound techniques. The specialist will discuss what assessments are required and when these should be done.

Osteoporosis is a difficult disease to treat once it is established and often the most that treatment can achieve is to stop any further deterioration of the bones. Several treatment options are available to manage osteoporosis, if needed. Treatment options are best discussed with the doctor.

Ankle Swelling

Some children with Turner Syndrome have swelling of hands or feet, due to lymphoedema or poor lymphatic drainage. In some, this may persist into adulthood although in most girls the problem slowly resolves. Once oestrogen replacement therapy has started, the retention of fluid in the tissues can sometimes increase. If simple remedies, such as raising the end of the bed are unhelpful, treatment options such as diuretics or specialised support stockings should be discussed with the doctor.

Social and Psychologic Problems

Some women find coping with the implications of Turner Syndrome harder than others. This may depend on their particular situation, or the attitude shown to them when they are growing up. Sometimes girls or young women who are relatively small for their age and who look immature are treated according to the size and not their age. This can cause feelings of loss of achievement and self-esteem which may result in a sense of being unable to succeed at anything.

Many of the problems which are associated with Turner Syndrome are seen first in childhood but continue into adulthood. They include difficulties with planning skills, problem solving and a certain lack of flexibility of thinking about day to day concerns.

There are also the emotional difficulties of coming to terms with being small as well as the lack of functioning ovaries, both implications of Turner Syndrome. Feeling 'different' because of these reasons and perhaps because of a slightly inflexible way of thinking means a woman may require professional help and advice. Comprehensive psychological care may often be necessary for women with Turner Syndrome who have a markedly impaired sense of self-esteem, as well as an inability to cope with daily events. Appropriate specialist care should be sought for women who are very dissatisfied with themselves and their lives.

Autoimmune disorders

Due to a generally increased life time risk for any of these disorders, your specialist will do routine tests for these problems every 1–2 years.

Coeliac Disease

5–10% of girls and women with Turner Syndrome may develop this condition, which is a disorder of poor food absorption due to gluten intolerance. A blood test will give an indication if it is present and the specialist will arrange treatment.

Glucose Intolerance

There is an increased risk of women with Turner Syndrome developing diabetes mellitus and it is therefore recommended that glucose levels are monitored annually.

Hypothyroidism

There is an increased risk of women with Turner Syndrome developing an underactive thyroid gland. It is therefore recommended that hormone levels are monitored annually.

Inflammatory bowel disease

Inflammatory bowel disease occurs more commonly in Turner Syndrome. This should be tested if there is chronic abdominal pain, diaorrhoea or bleeding from the bowel.

Features of Turner Syndrome

The following lists the features associated with Turner Syndrome. It is very important to remember that it is unlikely for any girl to have all these problems. The physical characteristics do not change markedly throughout life.

Features

(in alphabetical order not order of importance or frequency)

- **Broad chest with widely spaced nipples**
- **Coeliac disease** (gluten intolerance)
- **Constriction or narrowing of the aorta** (coarctation)
- **Cubitus Valgus** (increased carrying angle of the elbows)
- **Diabetes mellitus**
- **Droopy eyelids** (ptosis)
- **Dry skin**
- **Eczema**
- **Feeding difficulties in early life** (usually associated with the high arched palate)
- **Folds of skin on the ridge of the eye**
- **Gastrointestinal problems**
- **Hearing problems**
- **Heart murmur** (usually due to an abnormality of a heart valve)
- **High blood pressure**
- **Hypothyroidism** (reduced thyroid function)
- **Infertility**
- **Keloid formation** (formation of raised scar tissue)
- **Kidney and urinary tract problems**
- **Learning difficulties**
- **Long-sightedness** (hypermetropia)
- **Low hairline**

- **Low-set ears**
- **Lymphoedema** (build-up of the fluids on the limbs)
- **Micrognathia** (small jaw)
- **Narrow high arched palate**
- **Non-functioning ovaries**
- **Pigmented naevi** (moles)
- **Recurrent middle-ear infections**
- **Short fingers and toes**
- **Short-sightedness** (myopia)
- **Short stature**
- **Soft spoon-shaped nails which turn up at the tips**
- **Squint**
- **Webbed neck**

Questions and Answers

Is a girl with Turner Syndrome a true girl?
Yes, in every way. The only difference is that she will need long-term replacement of the hormones, which the ovaries normally make, to bring about the physical changes from girl to woman and to maintain good health in adulthood.

Will a girl with Turner Syndrome be able to have normal sexual relations when she grows up?
Yes, exactly the same as for any other women. The vagina and uterus are entirely normal in women with Turner Syndrome.

Will a girl with Turner Syndrome be able to have children?
This is unlikely without medical help. Through specialised fertility techniques, and by using a donated egg from another woman, it is possible. This needs to be discussed with the specialist.

Is the oestrogen and progestogen treatment the contraceptive pill? If so, why is the contraceptive pill used when a girl with Turner Syndrome is not fertile?
This aspect of treatment often causes the most confusion. A girl with Turner Syndrome needs replacement treatment of oestrogen and progestogen as her ovaries cannot supply these normally. The combination of hormones used is similar to that used in contraceptive pills. The type of oestrogen is often different from the contraceptive pill in order to lower the risk of high blood pressure that can occur with this treatment. Some doctors do use the regular contraceptive pill for girls with Turner Syndrome. As every girl is an individual, details of the exact

hormone replacement regime used needs to be discussed with the specialist.

Should medical checks be done throughout oestrogen replacement therapy?

Yes. A girl with Turner Syndrome should see the doctor about every six months to have blood pressure and weight checks. Blood pressure should always be measured in the right arm. If she has heart or kidney problems, then these checks may have to be made more frequently and this is something the specialist will discuss.

Does Turner Syndrome affect intelligence?

No, intelligence is across the normal range. There may be aspects of learning which present more difficulties, particularly abstract thought and reasoning connected with areas such as mathematics, but this can be made up for by increased skills in other areas.

Does a girl with Turner Syndrome have any special educational requirements?

There may be specific learning difficulties, which can be quite subtle and difficult to identify, but if it is felt that she is not fulfilling her potential, the specialist may be able to write to the school and arrange for an assessment. Extra help on a one-to-one basis, where it is particularly needed, can make an enormous difference to the progress made by a girl with Turner Syndrome.

Are there any other difficulties?

There may be behavioural problems, which may be distressing for the child as well as being difficult for those around them. The need for professional help should be discussed with the specialist.

Is there a normal life-span for a woman with Turner Syndrome?
Yes.

Can growth hormone cause diabetes?
Although growth hormone does have an anti-insulin effect, blood glucose levels should remain normal during treatment with growth hormone. In someone with a predisposition to diabetes mellitus, growth hormone treatment may be a factor in the timing of the onset of diabetes, but does not cause diabetes.

What are the likely main problems for a woman with Turner Syndrome?
Hopefully, if the diagnosis is made early, short stature will be less of a problem with the early initiation of treatment. As oestrogen is not produced by the non-functioning ovaries, oestrogen replacement will be needed from around the age of 11–13 years and will be continued throughout adult life. The main medical problems in adulthood will be the prevention of osteoporosis and the treatment of infertility, and management of hypertension and review of the aorta size, see page 23–24.

When should a girl with Turner Syndrome be told about her diagnosis and the full implications of Turner Syndrome?
It is best to be as open as possible to discuss the condition of Turner Syndrome from the earliest age. Even if it is believed that she is too young to understand the implications, this is often the best time. As she gets older she can ask questions suitable for her age and stage of development. Parents often find it difficult to discuss the subject but it can be started through simple explanations of why she is receiving medication. Any secrecy about the problem can lead to anxiety for the child and the parents.

Do women with Turner Syndrome need to continue seeing a doctor regularly?
Yes, particularly to make certain that she has adequate oestrogen replacement and that she is screened for the development of osteoporosis, high blood pressure, development of heart problems, diabetes, coeliac disease or an underactive thyroid gland.

If a girl with Turner Syndrome is having oestrogen replacement treatment why must she have periods?
Taking oestrogen alone without a progestogen (unopposed oestrogen) results in a build-up of the lining of the uterus which can, after a considerable time, increase the risk of cancer of the uterus. It is therefore important that she has regular withdrawal bleeds in order to keep the uterus healthy.

What is HRT?
The initials stand for hormone replacement therapy and this treatment involves the administration of oestrogen and progestogen in a way that mimics the body's normal secretion. A sequence of pills containing differing levels of oestrogen and progestogen are taken during the month, which continues the beneficial effects of these hormones once their normal levels decrease after the ovaries have stopped working (the menopause) or where ovaries have never worked (e.g. Turner Syndrome).

Is oestrogen therapy related to breast cancer?
This is a controversial subject and there are some ongoing concerns. However, if there is a risk, it is thought to be very small. Young women need oestrogen. Generally women who use the contraceptive pill do not have an increased risk of breast cancer. Rather, the risk relates to the total

length of exposure of the breast to oestrogen. If there are concerns about this, ask the specialist for further information.

Which method of HRT would suit a girl with Turner Syndrome and how long does she need to take it for?
This should be tailored to the individual and she will need to continue taking HRT until she reaches menopausal age. This needs to be discussed with the specialist.

Are there are other advantages to HRT other than the prevention of osteoporosis?
Yes, as well as maintenance of the female physical characteristics of puberty and moistness of the vagina, there is also a general improvement in well-being that is difficult to quantify. In addition, there is a significant reduction in the incidence of heart disease.

If a girl with Turner Syndrome has diabetes mellitus (sugar diabetes), will HRT interfere with this?
It may mean that her insulin treatment will need to be increased a little but it will make very little difference overall. Many women with Turner Syndrome have glucose intolerance which, in the majority of cases, is controlled by diet and HRT should not affect this.

If a woman with Turner Syndrome has IVF with a donor egg, will the baby be normal?
There is approximately a 1% chance in any pregnancy that the baby may have an abnormality. From the evidence available, it seems that the risk is no greater when having IVF or GIFT.

Does a girl with Turner Syndrome need to be monitored for the development of osteoporosis?
Osteoporosis might be an issue in later adulthood but with modern treatment and maintenance of HRT the risk is low.

How do you select a specialist who deals with Turner Syndrome in adults?
If a woman with Turner Syndrome is not already under the care of a specialist, this should be discussed with her GP. The Turner Syndrome support group or the specialist she saw for her paediatric care, can also offer advice.

Does a woman with Turner Syndrome need to be monitored for any hormone deficiencies?
Yes, thyroid hormone deficiency (hypothyroidism) is common in all adult women but especially those who have Turner Syndrome. This will require a blood test at intervals that the specialist will advise.

Glossary

Biosynthetic Hormone
Manufactured hormones that are identical to or perform the same function as those made naturally by our bodies.

Chromosome
A thread like structure that carries genetic information in the form of genes composed of DNA. Normally, each human cell contains 23 pairs of chromosomes and one pair of these are the sex chromosomes. Genes and chromosomes are like blueprints for the body's development, and so play a large part in determining a person's characteristics.

Coarctation of the Aorta
Narrowing of the main artery leaving the heart.

Diuretic
Any agent that increases the amount of urine excreted.

Endocrine Gland
A gland that makes hormones and releases them into the blood. The pituitary, thyroid, adrenal, testes (testicles) and ovaries are all endocrine glands. All of the glands together make up what is termed the endocrine system.

Endocrinologist
A doctor who specialises in the disorders of the endocrine glands.

Gamete intra-Fallopian Transfer (GIFT)
A technique where the egg and sperm are transferred into one of the fallopian tubes to allow fertilisation to take place naturally within the fallopian tube.

Growth Hormone
A hormone released by the pituitary gland, which promotes growth.

Hormones
Blood chemicals that stimulate growth and sexual development and help to regulate the body's metabolism. Normally the body carefully controls the release of hormones, as too much or too little may disrupt the body's delicate balance. They are produced by endocrine glands and carry messages from one cell to another via the bloodstream.

Hypertension
High blood pressure.

Intrauterine
Within the uterus (womb).

In Vitro Fertilisation (IVF)
The process of fertilising a woman's egg outside her body, allowing it to grow and inserting it back in her body.

Karyotype
The chromosome set of an individual. For example the karyotype of a girl with Turner Syndrome is usually 45X.

Lymphatic system
Small vessels under the skin that drain away body fluids.

Menopause
Permanent cessation of the menstrual cycle.

Oestrogen
A group of female hormones that are produced mainly by the ovaries from the onset of puberty and continuing until menopause, which controls female sexual development.

Osteoporosis
A condition that is characterised by thin, brittle bones.

Paediatric Endocrinologist
A doctor who specialises in the disorders of endocrine glands in children.

Placenta
The organ which connects the foetus to the wall of the uterus. The placenta provides the foetus with nourishment and eliminates wastes.

Progesterone
One of the female hormones that is produced mainly by the ovaries from the onset of puberty and continuing until menopause, which controls uterine bleeding.

Ptosis
Drooping eyelids.

Subcutaneous Injection
An injection given beneath the skin.

Syndrome
A syndrome is a collection of characteristics that occur together and characterise a particular condition.

Uterus
Womb.

X Chromosome
The female sex chromosome.

Y Chromosome
The male sex chromosome.

Support Organisations & Further Reading

The Association of Genetic Support of Australasia
www.agsa-geneticsupport.org.au

Australasian Paediatric Endocrine Group (APEG)
www.apeg.org.au

The Endocrine Society
www.endo-society.org

The Hormone Foundation
www.hormone.org

The Magic Foundation
www.magicfoundation.org

Parent and Family Resource Centre NZ
www.parentandfamily.org.nz

Parent to Parent NZ
www.parent2parent.org.nz

UK Society for Endocrinology
www.endocrinology.org

Turner Syndrome Association of Australia
www.turnersyndrome.org.au

Turner Syndrome Support Group NZ
www.turnersyndrome.co.nz

UK Child Growth Foundation
www.childgrowthfoundation.org

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Merck Serono is proud to bring you this booklet from the *Hormones and Me* educational series. We aim to provide readers with a better understanding of the issues relating to endocrine disorders particularly in children. We hope that you find it a valuable and helpful resource.

Please ask your doctor or nurse for further information on the resources available to you.

The ***Hormones and Me*** series includes:

1. Growth Problems in Children
2. Turner Syndrome
3. Craniopharyngioma
4. Diabetes Insipidus
5. Puberty and its Problems
6. Delayed Puberty
7. Multiple Pituitary Hormone Deficiency (MPHD)
8. Congenital Adrenal Hyperplasia (CAH)
9. Growth Hormone Deficiency in Adults
10. Management of Emergency or 'Stress' Situations where Hypoglycaemia or Cortisol Deficiency Occur
11. Intrauterine Growth Retardation (IUGR)
12. Congenital Hypothyroidism
13. Klinefelter Syndrome

DISCLAIMER

Speak to an appropriate healthcare professional

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Connections for Growth

Hormones and Me

Turner Syndrome

This booklet is valuable reading for girls and women with Turner Syndrome.

It is also recommended reading for their family and friends.

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