Considering Pregnancy?

Information for women with Turner Syndrome

The Bungle Pack

kindly supported by **Tracey and Lainey Walters**

in memory of

Corporal James Walters

affectionately known as **'Bungle'**

TSSS

Turner Syndrome Support Society

The Turner Syndrome Support Society (TSSS) is proud and very grateful to have produced 'The Bungle Pack', in memory of James Walters, affectionately known as 'Bungle'.

"James was extremely passionate about TS and made sure that we were as prepared as we could be for all aspects of Lainey's condition. He would be immensely proud and completely overwhelmed at how far his baby girl has come, and to know that the money raised in his memory is making a difference, by educating parents, saving TS girls' lives and supporting individuals with TS, their families and healthcare professionals."

Tracey Walters

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This booklet is written for healthcare professionals involved in the care of the woman with Turner syndrome (TS) who is considering pregnancy.

Pregnancy may impose serious risks for both the mother with TS and her unborn child. The aim of this booklet is not to provide medical guidance, but to include some helpful background information to support discussions between healthcare professionals, the woman and her partner.

Overview of Turner Syndrome

Turner syndrome (TS) is a relatively common chromosome abnormality affecting only females. In classical TS the girl has only one X chromosome in her cells (45X karyotype). Alternatively, the girl has some cells in her body with two X chromosomes, but other cells have only one, and this is called mosaicism.

There is wide variability in the severity of clinical features between individuals (Donaldson et al 2006). Although textbooks often refer to the marked phenotype (physical characteristic) that is evident at birth, many girls with TS are diagnosed after the age of puberty, or even as adults, which reflects the increasingly recognised mild phenotype.

Although TS is a lifelong condition, most individuals live long and healthy lives, but some may have several associated long-term conditions which require routine medical screening, regular monitoring, and follow-up.

Cause of TS

The exact cause of TS is unknown. TS appears to occur as a random event during cell division, early in the development of the fetus. It is not usually inherited and the age of the mother does not increase the risk of TS. There are no clearly established risk factors and the recurrence of TS in subsequent pregnancies is rare.

Incidence and prevalence

TS occurs in approximately 1 in every 2000 to 1 in every 2500 live female births (Nielsen et al 1991). The true prevalence of TS is difficult to ascertain for many reasons; for example some individuals have a mild phenotype and may remain undiagnosed. TS occurs with more or less the same prevalence in all ethnic groups and in different countries.

Medical problems

TS may present the girl/woman, the family and the healthcare team with a wide range of genetic, developmental, endocrine, cardiovascular, psychosocial, and reproductive issues. More than 95% of adult women with TS have short stature (Saenger et al 2001) and over 90% will have signs of ovarian failure (Bondy 2007). The range of other associated long-term conditions includes cardiovascular disease, hypertension, obesity, type 2 diabetes, hypothyroidism, sensorineural hearing loss, and osteoporosis.

Pregnancy and Turner syndrome

Pregnancy may be possible naturally for the woman with TS, but only if ovarian function is conserved. Natural pregnancy occurs in 2-8% of women with TS (Bernard et al 2016) but high rates of miscarriages, stillbirths and a risk of fetal chromosomal abnormalities may occur (Bernard et al 2016, Karnis 2012).

For the majority, oocyte donation (OD) and in vitro fertilisation (IVF) is the only way to become pregnant (Cabanes et al 2010). The pregnancy rate after OD is high and women with TS appear to have the same chance of success as other women. However, these pregnancies are associated with many complications, including an increased risk of miscarriage and maternal death from aortic dissection or tear in the wall of the aorta, and pre-eclampsia (Chevalier et al 2011, Hewitt et al 2013). The risk of maternal death has been estimated at 1-2% (ASRM 2012, Chevalier et al 2011).

Spontaneous or medically-assisted pregnancy for women with TS should be undertaken only after cardiac evaluation and counselling.

Risks of pregnancy

The increased demands of pregnancy pose serious risks for women with TS who may have cardiovascular malformations and an intrinsic aortopathy or disease of the aorta, as well as other concurrent risk factors such as hypertension, diabetes, and obesity (Bondy 2007, Cabanes et al 2010, Karnis 2012).

The cardiovascular abnormalities that occur in women with TS include coarctation or narrowing of the aorta, a bicuspid aortic valve, where the valve has only two cusps rather than three, and an enlargement of the ascending aorta (ASRM 2012). In pregnancy there may be a worsening of pre-existing hypertension, pre-eclampsia or aortic dissection (tear in the aorta) which may be life-threatening (Delabaere et al 2002, Karnis 2012).

The risk of aortic dissection or rupture during pregnancy in women with TS is approximately 2%; rupture of the aorta is life-threatening for both mother and child (ASRM 2012). The risk factors for dissection include bicuspid aortic valve (with or without aortic enlargement), coarctation (whether or not it is repaired) and hypertension (Cabanes et al 2010, Delabaere 2002, Karnis 2012), with 50% of aortic dissections reported in the literature occurring in the third trimester or post-partum. Women with TS appear to be at a higher risk of aortic dissection during pregnancy than other individuals with bicuspid aortic valve and coarctation of the aorta, as the associated aortopathy appears to be more aggressive.

Women with TS should be screened for gestational diabetes and some may have existing hypothyroidism.

Premature delivery of the baby may be required because of hypertension, gestational diabetes or hepatic complications. Delivery is often by Caesarean section (C-section) because of the short stature of most women with TS. Under optimal conditions, spontaneous vaginal delivery is an acceptable option, but the likelihood of a C-section is increased because of small stature, cardiovascular disease, hypotensive disorders and intrauterine growth restriction (Karnis 2012).

Overview of pregnancy risks

- Cardiovascular:
  - dilatation and possible dissection or rupture of the aorta which is life-threatening for both mother and child
  - hypertension and pre-eclampsia
- Metabolic: gestational diabetes
- Hepatic: cholestasis (reduction or stoppage of bile)
- Obstetric: maternal short stature requiring Caesarean section

Fertility counselling

Counselling about fertility should be regarded as an integral part of the management of a woman with TS. Infertility can be very distressing and counselling provides an opportunity for the woman and her partner to explore their thoughts, feelings, beliefs and their relationship in order to reach a better understanding of the meaning and implications of any choice of action they may make. Counselling will also provide support if they undergo treatment and may help them to accommodate feelings about the outcome of any treatment. Counselling should be non-directive and the facts explained as clearly as possible, providing the woman and her partner with accurate information about her infertility, the risks of pregnancy, the need for pre-pregnancy assessment, conception methods available and the close monitoring required if pregnancy is successful.

Pre-pregnancy counselling

Pre-pregnancy counselling should involve consultation with the interdisciplinary team particularly cardiology, endocrinology, and genetics. All aspects of the consequences of pregnancy need to be discussed, allowing the woman and her partner to make an informed choice. Those women who have had normal cardiac imaging at their pre-pregnancy assessment should also be thoroughly counselled regarding the risk of cardiac complications during pregnancy. Aortic dissection may still occur following normal cardiac imaging, resulting in maternal and fetal death, or require life-saving emergency aortic surgery which carries a 30% risk of fetal death.

Key notes for women with TS considering pregnancy

- Spontaneous pregnancies are rare: in most cases egg donation and *in vitro* fertilisation is the only way to become pregnant (and may not be available on the NHS)
- Pregnancy, either spontaneous or medically assisted, has a high risk of complications:
  - cardiovascular:
    - dissection or rupture of the aorta (life-threatening for both mother and child)
    - hypertension and pre-eclampsia
  - metabolic: gestational diabetes
  - hepatic: cholestasis (reduction or stoppage of bile)
  - obstetric: short-stature requiring Caesarean section
- Pre-pregnancy medical assessment is required

Pre-pregnancy medical assessment

A thorough pre-pregnancy assessment is required to review the woman's medical status involving the interdisciplinary team, particularly the cardiologist and endocrinologist. The woman's general health will be reviewed including weight, body mass index and whether they smoke.

Pre-pregnancy assessment

- Cardiologist: measure blood pressure, ultrasound and MRI imaging of the heart
- Endocrinologist: test for diabetes, thyroid abnormalities, liver disease, and kidney disease

Methods of conception

Depending on the medical assessment, women with TS who have spontaneous menstrual cycles and ovulate normally should be advised not to postpone pregnancy because of the risk of premature ovarian insufficiency.

For those woman without functional ovaries, OD and IVF can be used. Adequate hormone replacement therapy is required to increase the size and blood flow to the uterus prior to egg or embryo transfer. Transferring only one embryo at a time to the uterus will minimise the risk of twin pregnancies.

It is important to note that, depending on individual circumstances, OD and IVF may not be available on the National Health Service in the UK. Adoption may be an option for many women with TS, and the use of surrogate mothers may be an option in some countries.

Pregnancy monitoring and delivery

For those who decide on pregnancy, and if conception is successful, careful observation, increased cardiac monitoring with repeated cardiac imaging and frequent evaluation is required involving the specialist interdisciplinary team, for the duration of the pregnancy and also post-partum. Women with TS should be advised that if they develop pain in the chest, back or shoulder-blade, they should attend hospital immediately. Good control of blood pressure is important; women taking treatment for hypertension should be advised of the importance of taking their medication. Delivery of the baby must take place in a specialist centre with access to all the expertise required.

Future methods of conception

In the future ovarian tissue from young girls with TS could be cryopreserved for infertility treatment, however, the optimum methods for stages of this process are still being developed. Oocyte preservation using a rapid freezing technique may also be available in the future for some women with TS.

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Further information

Turner Syndrome Support Society
www.tss.org.uk

Turner Syndrome International Group
www.tsint.org

Turner Syndrome Support Society UK
12 Simpson Court,
11 South Ave, Clydebank Business Park, Clydebank G81 2NR
Tel: 0141 952 8006
Fax: 0141 952 8225
Helpline: 0300 111 7520
Email: Turner.syndrome@tss.org.uk
Website: www.tss.org.uk
(Charity Reg. ENG108057 SCO37932)

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