Having an extra sex chromosome is actually a fairly common event. It's often unnoticed because the effect of an extra X or Y does not lead to the same severe consequences as an extra chromosome in the other pairs (as in Down or Edward syndrome). However, extra sex chromosomes can increase the chance of physical abnormality or learning disability and may be associated with later fertility problems.

With the exception of Turner syndrome, antenatal detection of a sex chromosome anomaly in a fetus or baby is often a chance finding, perhaps as a result of antenatal testing. When the situation arises, it can pose challenging issues for parents and staff alike as problems need to be discussed and decisions made about the future.

**Turner syndrome**

Turner syndrome involves a lack of one X chromosome in a female, giving a total number of 45 chromosomes instead of the normal 46. The lost chromosome is usually from the father. Advanced paternal age is associated with the condition. Some key features of the syndrome are shown in the box.

The prevalence in liveborn females varies between 1 in 3000 to 5000 livebirths, although it isn’t clear how much this has been affected by improvements in antenatal detection.

The miscarriage rate is reported to be very high with over 95% of cases lost in early pregnancy. 10% of all miscarriages in the first 12 weeks may be due to Turner syndrome.

70 cases were reported to CARIS from 1998-2002, giving a gross rate* in Wales of 9.1 per 10,000 female births. Of the 70 cases, 17 (24%) were fetal losses, reflecting the known high miscarriage rate. Pregnancy was terminated in 37 (53%) cases and 16 (23%) were liveborn. This means that in Wales over the past 5 years, 1 in 4782 liveborn girls have been affected by Turner syndrome, in keeping with expected levels. Of the 16 liveborn cases, 14 (88%) were still alive at the end of the first year of life.

**Antenatal diagnosis**

In Turner syndrome the lymphatic vessels at the back of the neck often become blocked. This causes an accumulation of fluid behind the neck called a cystic hygroma. The fluid may be more widespread and show up as generalised swelling or hydrops of the fetus. It has been estimated that up to 70% of fetuses with a cystic hygroma will turn out to have Turner syndrome.
Of the 70 cases of Turner syndrome reported to CARIS, 49 (70%) were detected before the 24th week of pregnancy and in 35 of these, the pregnancy was terminated. For the remaining 2 terminated cases, termination was undertaken because of other anomalies and Turner syndrome was diagnosed after the end of pregnancy.

Forty cases were reported to have a cystic hygroma (57%) and 27 (39%) had hydrops/oedema on antenatal ultrasound. 8 further cases showed some enlargement of the nuchal area. Ultrasound findings suggested cardiac anomalies in 6 cases.

As the outlook in pregnancy is poor it is not surprising that in 11 of the 70 cases no fetal heart activity was seen on ultrasound scan.

Postnatal Diagnosis
Infant blood was sent for karyotype in 13 cases, the indications being clinical suspicion (3), follow up to confirm the antenatal result (3), and others including speech delay, short stature and failure to thrive.

Anomalies associated with Turner syndrome
Published reviews suggest that cardiac anomalies are seen in 15% of fetuses, coarctation of the aorta being the most common. Renal anomalies are seen less often and include hydronephrosis, renal hypoplasia and renal agenesis.

For the 70 cases reported to CARIS, 46 (66%) had some form of additional congenital anomaly, apart from cystic hygroma/hydrops. Circulatory system defects were present in 25 cases (36%), 15 of which involved problems in the development of the aorta. Urinary defects were present in 14 cases (20%). Poor lung development was another common feature, particularly in fetal losses.

Klinefelter syndrome
Klinefelter syndrome originates at an early stage of cell division when an error in splitting of the parental sex chromosomes results in an extra X chromosome in the fetus, either from the mother or father. The risk increases with maternal age.

This is one of the commoner chromosomal abnormalities with a reported prevalence rate of between 1 in 500 to 800 liveborn males. However, the majority of cases are not diagnosed for several years and sometimes the condition may never be recognised.

For the years 1998 – 2002, 14 cases of Klinefelter syndrome have been reported to CARIS. Nine of these were liveborn so that about 1 in 9,000 liveborn boys in Wales were known to be affected. Comparing this to the generally accepted rate, it is likely that 9/10 cases of Klinefelters are unrecognised during the first year of life. Five cases were terminated, one of whom also had Edward syndrome. All 9 liveborn cases survived to the end of their first year.
The presence of the extra X chromosome has a feminising effect on an otherwise male child, leading to many of the typical features of the condition. Infertility and learning difficulties are two of the more significant consequences.

### Antenatal Diagnosis
Klinefelter syndrome is not associated with early pregnancy problems. Many cases are never diagnosed as there are no specific structural abnormalities.

Of the 14 cases in Wales, only 3 scan anomalies were reported. Interestingly, 3 mothers received Down syndrome screening results in the high risk range.

### Postnatal Diagnosis
4 cases had infant blood karyotypes, the indications being congenital anomaly and developmental delay.

### Associated Anomalies
Relatively few other anomalies were reported for cases of Klinefelter syndrome, apart from 1 case with additional chromosomal defects. Three cases were diagnosed as having cardiac septal defects.

### Other Sex Chromosome Anomalies
31 further cases were reported to CARIS including triple X syndrome (7 cases) and XYY syndrome (7 cases). The majority of these (25) were liveborn and most were known to have survived their first year.

### Klinefelter syndrome
- **Chromosomes:** 47 XXY
- **Occurrence:** 1/500-800 male livebirths
- **Phenotypic sex:** Male
- **Gonads:** Atrophic testes
- **Fertility:** Infertile
- **Intelligence:** Normal/Slightly reduced
- **Other features**
  - Poor facial hair
  - Tall stature
  - Gynaecomastia
- **Treatment:** Testosterone from puberty

### Triple X syndrome
- **Chromosomes:** 47 XXX
- **Occurrence:** 1/1200 liveborn females
- **Phenotypic sex:** Female
- **Gonads:** Normal
- **Fertility:** Usually reduced
- **Intelligence:** Usually reduced
- **Other features**
  - Tall stature
  - Learning difficulties
  - Possible early menopause
- **Treatment:** None

### XYY syndrome
- **Chromosomes:** 47 XYY
- **Occurrence:** 1/1000 liveborn males
- **Phenotypic sex:** Male
- **Gonads:** Normal
- **Fertility:** Normally normal
- **Intelligence:** Usually normal
- **Other features**
  - Tall stature
  - Learning difficulties
  - Possible severe acne
- **Treatment:** None

### Counselling in Sex Chromosome Anomalies
Giving parents any abnormal test result requires great care and sensitivity. Though sex chromosome anomalies appear to be quite common, clinicians may find it difficult to explain the implications of the diagnosis.

In the antenatal period the ultrasound and serum screening processes are in search of more serious conditions. After birth subtle changes in the baby such as developmental delay may prompt a request for a karyotype. A result may be negative for a serious chromosomal disorder but show a problem with the sex chromosomes. The parents deserve that this information is handled with the utmost care and it is essential to give honest informed advice.
A recent study looked at what parents were told after a prenatal diagnosis of a sex chromosome abnormality. They found great variation in how, where and who gave the information, with some examples of misleading or inaccurate counselling. Health professionals involved in this work need to be properly informed of the nature of sex chromosomal syndromes and their likely outcomes.