

## The Genetics of PWS

### Introduction

PWS is a complex genetic syndrome and research is uncovering many variations within it. This information reflects current knowledge, and therefore may change over time, as more research is carried out.

It is important to remember that neither parent is to blame for PWS affecting their child – it is an accident of nature which could not have been prevented or caused by actions on the part of either mum or dad.

### Genetic types of PWS

Current research has shown that the set of symptoms known as Prader-Willi Syndrome result mainly from one of 4 different genetic abnormalities. These are:

Either: 1. A small deletion on chromosome 15.

Or: 2. Chromosome 15 maternal disomy.

Or: 3. A translocation of chromosomes involving chromosome 15.

Or: 4. An error in the imprinting of chromosome 15.

#### 1. A small deletion on chromosome 15

Approximately, 60-70% of PWS cases are due to a de novo (or new) deletion (loss of a small part) of the chromosome 15 inherited from the father. There has been no known recurrence in any of these families. Theories have been put forward that this is due to accidental damage to the sperm prior to conception, but none of these have yet been proved conclusively.

#### 2. Maternal disomy

In about 25-30% of cases, Prader-Willi Syndrome can be the result of maternal disomy (two copies of chromosome 15 coming from the mother instead of one copy from each parent). These are included in the **non-deletion** cases. Once again there has not been a known recurrence of maternal disomy in any PWS family. However, the recurrence risk here is usually given as 0.4% for two reasons. Firstly, because some non-deletion PWS may be due to something other than disomy, and secondly because the risk of disomy increases a little with maternal age. Like the deletion cases, disomy is an accidental occurrence which occurs at meiosis (the process of cell division which takes place prior to conception).

#### 3. A translocation of chromosomes involving chromosome 15

The very few families (less than 5%) which do have a high risk of having more than one child with PWS are those which carry a translocation involving chromosome 15. A translocation is an exchange of material between or within chromosomes, and can involve any chromosome, not just 15. When the translocation is **balanced** then it can pass from one generation to another with no harmful effect, but it is sometimes possible for it to be passed on in an **unbalanced** form, and a deletion can result.

When a deletion on the father's chromosome 15 is the result of a translocation or structural rearrangement involving chromosome 15, then the recurrence risk can be high. The actual risk in individual families depends upon the rearrangement which they carry. Fortunately however, cytogenetic studies can identify these families so that they can receive appropriate advice.

#### **4. An error in the imprinting of chromosome 15**

Chromosome 15 carries an imprinted region. The result of this abnormality of imprinting is that the genetics of the affected child is rather similar to having a maternal disomy.

#### **How likely is PWS to occur again in a family?**

In the vast majority of cases, the risk of having another child with PWS is very slight indeed. For example, a study in Australia of 144 families with a child with PWS found no recurrence. There were 266 living siblings of the PWS children, and none had the condition.

However, if the child is diagnosed with the imprinting error or translocation type of PWS, a geneticist can explain the likelihood of recurrence.

#### **Are there any physical or mental differences between the types?**

Research is continuing into whether there are any differences in development between those who have a deletion and those who do not and those with an imprinting error. Although there appears to be little difference with regard to the major characteristics of PWS, differences have been found with regard to some aspects of cognition, physical appearance and mental health, which could be important to be aware of. However, there is no feature that is exclusively found in one of these three genetic categories. See more about the difference between the types from the [International PWS Organisation](#).

#### **How is testing carried out?**

Taking blood samples is part of the initial diagnosis procedure in PWS. A sample is taken from the child or adult with PWS in the first instance. Chromosomes and DNA are both obtained from the white cells. Anyone suspected of having PWS should be tested with a **DNA methylation analysis**. This test detects nearly all (>99%) cases of PWS.

(It also detects Angelman syndrome which involves the same region of chromosome 15 but in the case of Angelman syndrome any deletion affects the mother's chromosome 15 or it is due to a paternal chromosome 15 disomy.)

For further information on testing see [Getting tested \(USA\)](#) - Brief description of deletion, disomy and imprinting and the tests which can be used in diagnosis.

#### **Further information**

[The Genetics of PWS – An explanation for us all](#) (PWSA USA) Description of the genetics involved in PWS including genomic imprinting, and the range of genetic tests which can be used in diagnosis.