PRADER-WILLI SYNDROME

1. What is Prader-Willi Syndrome?

Prader-Willi Syndrome (PWS) is a condition caused by an abnormality on one of our chromosomes, specifically the chromosome 15. Children with PWS are born with floppy muscles and have severe feeding difficulties and poor weight gain in the first year of life. However, by the time they are three years old, they develop a voracious appetite. This can lead to rapid weight gain and obesity, even in early childhood. Children with PWS may also have learning difficulties and behavioral problems.

2. Who gets PWS?

About 1 in every 15,000 births is affected by Prader-Willi Syndrome. It occurs in both boys and girls and people of any ethnic background can be affected by it.

3. What causes PWS?

Prader-Willi Syndrome is due to missing or inactive genes in a specific region of one of an individual's two chromosome 15s, the one normally contributed by the father. This specific region of the maternal chromosome 15 is always inactive and therefore we depend only on the genes coming from the father.

The chromosomes are the packages of genes found in nearly every cell of the body. We have 46 chromosomes. The chromosomes come in pairs because we inherit one set from each parent. The genes that cause Prader-Willi Syndrome are on chromosome 15.

4. Is PWS inherited?

Most cases of PWS are not inherited - they are caused by a genetic error that occurs at or near the time of conception for unknown reasons. In a very small percentage of cases (1% or less), a genetic change that does not affect the parent is passed onto the child and in these families more than one child may be affected. All families in whom there is a person affected with Prader-Willi Syndrome should have the chance to talk to a geneticist or genetic counsellor.

5. What causes PWS?

Prader-Willi Syndrome occurs when a baby has failed to inherit some active genes from a specific region of his/her father's chromosome 15. There are three different ways that this can happen:

1. A small section of chromosome 15 is missing - a paternal deletion. This is the most common form of PWS. At the time of conception, something happens that causes a small part of the chromosome 15, which is inherited from the child's father, to disappear. This is called a chromosome deletion. It is unlikely to happen again in another pregnancy.

2. The baby has two copies of his/her mother's chromosome 15, called maternal uniparental disomy (UPD). This form of PWS occurs in about one in four cases. It happens when a baby is born with two copies of his/her mother's chromosome 15 and no copy of his/her father's chromosome 15. The effect is the same as a paternal deletion: the child is missing some genes from its father.

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3. The baby's PWS genes are 'switched off', this is called an 'imprinting' mutation. Rarely (in about one in twenty cases), the PWS genes on the father's chromosome are present, but they don't work properly and they seem to be 'switched off'. This is caused by a change (a mutation) in the gene on chromosome 15 that turns the PWS genes on and off. The process of turning these genes on and off is called imprinting. This rare type of mutation can be inherited or can start for the first time in an affected child.

6. What kind of problems do people with PWS experience?

Appetite and weight management: Children with Prader-Willi Syndrome have a huge appetite. They can become obsessed with food. The combination of eating too much and lack of physical activity can lead to rapid weight gain and obesity. Parents may find it difficult to prevent these children from eating too much. Weight control often requires strict restrictions on the child's access to food. This may mean locking the kitchen and food storage areas.

Behavior: Infants and young children with PWS are typically happy and do not have serious behavior problems. Older children and adults, however, do have behavioral problems. They find it particularly difficult to cope with changes in their daily routines. Behavioral symptoms such as: temper tantrums, stubbornness, obsessive behaviors, obsessive-compulsive disorder, skin picking or psychosis, usually start at about the same time as over-eating problems. Daily routines and a firm and structured environment seem to work best for behavior management.

Neurodevelopmental problems: Children with PWS usually learn to sit, walk and crawl later than other children. They can continue to have problems with strength, co-ordination and balance. Physical and occupational therapies help children to acquire these skills. Mild to moderate intellectual disability is a common feature of the disorder. In addition, affected children may show signs of global developmental delay and they appear to have an increased risk for seizures.

Feeding and speech problems: Weak and floppy muscles may cause feeding problems in young babies with PWS. Speech development is often delayed. The need for speech therapy should be assessed in infancy. In rare cases, speech is severely affected.

Education and learning: Children with PWS usually have learning problems. Like all children, they have strengths and weaknesses. They usually need special help at school.

Growth: Babies with PWS are often slow to gain weight initially and they may sometimes need tube feeding. Children with PWS benefit from treatment with growth hormone. The need for growth hormone therapy should be assessed by a pediatric endocrinologist.

Sexual development: Sex hormone levels (testosterone and estrogen) are usually low in Prader-Willi Syndrome. Both sexes have a good response to treatment for hormone deficiencies, although side-effects have been reported. Puberty usually starts late.

Sleep Apnea: Sleep apnea is a condition in which breathing pauses during sleep

7. How is PWS diagnosed?

Typically, Prader-Willi syndrome is suspected based on signs and symptoms. A definitive diagnosis can almost always be made through a blood test. This genetic testing can identify abnormalities in a child's chromosomes that indicate Prader-Willi syndrome.

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8. What is the treatment for PWS?

Although specific treatments vary depending on symptoms, most children with Prader-Willi syndrome will need the following:

- **Good nutrition for infants:** Many infants with Prader-Willi syndrome have feeding difficulties due to decreased muscle tone. Your child may need a high-calorie formula or special feeding methods to help gain weight.
- **Human growth hormone (HGH) treatment:** HGH treatment in children with Prader-Willi syndrome helps increase growth, improves muscle tone and decreases body fat. An endocrinologist can help determine whether your child would benefit from HGH and discuss any risks. A sleep study is usually recommended before starting growth hormone treatment.
- **Sex hormone treatment:** An Endocrinologist may suggest hormone replacement therapy (testosterone for males or estrogen and progesterone for females) to counteract the low levels of sex hormones. Hormone replacement therapy usually starts when a child reaches the normal age for puberty and can help reduce the risk of developing thinning of the bones (osteoporosis). Surgery may be needed to correct undescended testicles.
- **Weight management:** A dietitian can help you develop a healthy, reduced-calorie diet to help manage a child's weight while ensuring proper nutrition. A restricted-calorie diet may require supplemental vitamins or minerals to ensure balanced nutrition. Increasing physical activity and exercise can help manage weight and improve physical functioning.
- **Treatment of sleep disturbances:** Treating sleep apnea and other sleep problems can improve daytime sleepiness and behavioral issues.
- **Behavior management:** Setting strict limits on behavior, schedules and access to food and strict supervision of food intake may be required. Some patients may need medication to manage behavior problems.
- **Mental health care:** A mental health professional, such as a psychologist or a psychiatrist, may help address psychological problems, for example, obsessive-compulsive behaviors, skin picking or a mood disorder.
- **Other treatments:** These may include addressing specific symptoms or complications identified by eye exams for vision problems, tests for hypothyroidism or diabetes, and examinations for scoliosis.

9. Useful links for parents

https://www.pwsa.co.uk/what-is-pws