Prader-Willi Syndrome (PWS) was first described in 1956 by Swiss doctors, Prof. A Prader, Dr A Labhart and Dr H Willi, who recognised the condition as having unique and clearly definable features. These features are:-

- Hypotonia: weak muscle tone, and floppiness at birth.
- Hypogonadism: immature development of sexual organs and other sexual characteristics.
- Obesity: caused by excessive appetite and overeating (hyperphagia), and a decreased calorific requirement owing to low energy expenditure levels. (Obesity is not normally a feature of those whose food intake is strictly controlled.)
- Central nervous system and endocrine gland dysfunction: causing varying degrees of learning disability, short stature, hyperphagia, somnolence, and poor emotional and social development.

Many people with PWS also exhibit characteristic facial and other physical features. These include: almond-shaped eyes, a narrow forehead (measured across), a down-turned mouth with a triangular-shaped upper lip, and small hands and feet.

People with PWS have poor large muscle strength, often coupled with poor coordination and balance. Muscle tone can be improved with appropriate therapy and exercise. Small muscle strength is usually better.

Most people with PWS have borderline or moderate learning difficulties. Some people have recorded IQs of 90 or above, whilst a minority have severe learning difficulties. The average IQ is around 70 or slightly lower, although individuals may sometimes find it difficult to perform at their IQ level, as emotional and social skills are often less developed. Reading and writing skills are usually considerably better than number skills and abstract thinking. Individuals often excel at sedentary activities such as jigsaw puzzles, “wordsearches”, sewing, drawing and colouring.

Cause
PWS is caused by an abnormality on chromosome 15 which occurs around the time of conception. The majority of cases (about 70%) are caused by a deletion on the chromosome 15 inherited from the father, whilst about 25% are caused by inheriting two chromosome 15s from the mother, instead of one from the mother and one from the father (maternal disomy). A small minority of people have a translocation or imprinting irregularity involving chromosome 15. The recurrence risk of PWS in a family is very small. No blame attaches to either parent - currently PWS is thought to be a
purely accidental occurrence.

**Atypical PWS**

A few people have a PWS diagnosis, but do not have the typical physical features - in particular they may be much taller than usual, even without growth hormone.

**Acquired PWS**

PWS-like symptoms can be "acquired" by damage to the hypothalamus during a person's life or from a dysfunction of the hypothalamus. This may be as a result of a head injury, or from a tumour, or from surgery following the removal of a tumour, or from a dysfunction from birth. In these cases, the person does not have any of the genetic abnormalities and few of the physical characteristics of PWS, but acquires some or all of the behavioural and appetite problems which are associated with the syndrome. Management techniques used with people with true PWS can also be helpful in acquired PWS.

**Incidence and Prevalence**

An epidemiological study carried out in one health region in the UK in 2000 estimated birth incidence to be in the region of 1:22,000, with a lower bound for population prevalence of 1:52,000. Previous estimates have estimated a birth incidence between 1:10,000 and 1:25,000. Much of the uncertainty with regard to the statistics for incidence and prevalence is due to the fact that PWS may still go undiagnosed in some people.

**Stages of Development**

**Infancy**

Babies with PWS are very floppy at birth, and the ability to suck is weak or absent. Tube-feeding may be required for the first few days or weeks of life; breast-feeding is rarely initially successful. Babies show little interest in feeding during the first few months of their lives, have a very weak cry, and sleep for most of the time during the early weeks. Male babies may have noticeably underdeveloped genital organs. Female babies may also have underdeveloped genitalia, but this is much harder to detect. Developmental milestones such as sitting, standing, walking and talking are generally delayed, but most children with PWS are able to attain all these abilities by the time they are about 5 years old. Infants with PWS are very lovable and placid, and seem to draw admiration wherever they go.

**Childhood**

Some time between the ages of one and four years, children with PWS begin to show a heightened interest in food and in severe cases develop what appears to be an insatiable appetite, so that they will try to obtain food by any means possible. The degree to which this occurs varies considerably between individuals, but there is always a preoccupation with food in play and talk. This can be helped by good management, dietary control and educating the child about his or her diet.
However, if energy intake has not been carefully monitored, weight gain is rapid; hence, a lower calorie diet (energy controlled regime) is essential throughout the person's life. An appropriate exercise programme helps to keep weight levels down and also improves muscle strength. If weight is not controlled, fat accumulates in a characteristic way on the buttocks, stomach, lower trunk and thighs. Children with PWS are generally placid and friendly, but may begin to exhibit stubborn or obsessive behaviour, and outbursts of temper if they cannot get their own way or are denied access to food.

**Adolescence**
People with PWS do not usually reach full sexual development, and there have been only three cases worldwide of a woman with PWS having a child. However there may be cases of which doctors are unaware. People with PWS are individual in their growth pattern, and there is no set way in which they all develop. A minority start to develop sexually at a young age, but in the majority, puberty is delayed until the late teens. Men have a small penis, and undescended testes are common. Pubic and facial hair may be scanty, and voice change may not occur. In women, breast development is often small, and menstruation, if it occurs, may be irregular and/or scanty. Teenagers with PWS do not experience the growth spurt which usually occurs in the early teens and hence tend to be a few inches shorter than average: men average about 5'2" (155cm) and women average about 4'10" (145cm). Growth hormone treatment may be given to help with growth and muscle tone, and sex hormones (both male and female) to help with sexual development, but this will depend to some extent on the individual's existing hormone levels. Behavioural and eating problems may become more challenging during the teens and early twenties.

**Life as an adult**
As adults, people with PWS have varying abilities in attaining independence, although all will need some form of support or monitoring to help with controlling their food intake, and thus their weight. Despite the fact that many individuals have the intellectual and physical ability to work, they are usually ill-equipped on an emotional and social level to deal with the stresses and demands of the ordinary workplace. However, they can make a positive contribution to society in many ways and may be involved in voluntary work, craft work, or have a part-time job. Many people live with their families, but an increasing number are living in residential homes, or being supported to live in the community. In the past, life expectancy was short because of health problems associated with massive obesity, but nowadays life expectancy is increasing because of better dietary management and better understanding of the problems associated with PWS. The oldest known person with PWS in the UK is a woman aged 72. Whilst cancers and strokes are not so common in older people with PWS, mental health problems may increase with age.

**The Treatment of PWS**
Apart from various hormone treatments and some surgical intervention (eg, to bring
down undescended testes), there is no "cure" for PWS. There have been many advances in the fields of genetics, but it will be several years before the genes which are involved in PWS are fully identified. No drug so far has proved to be of lasting help with regard to suppressing appetite. Severe challenging behaviour and some mental health problems have responded relatively successfully to drug treatment, but dosages need to be carefully monitored. Generally speaking however, many of the adverse effects of the syndrome can be lessened by good dietary management, exercise programmes, good general health care, and by good general management of behaviour and education. The help of a dietitian, paediatrician, physiotherapist, educational psychologist, and (if necessary) speech therapist should be sought as soon as a diagnosis is made.