Prader-Willi Syndrome (PWS) – Information for GP's

Overview

Prader-Willi syndrome: rare genetic abnormality of Chromosome 15.

Characteristics

Hyperphagia:

- Voracious overeating leading to morbid obesity
- Food foraging - ingestion of inappropriate items needs to be considered
- Sometimes excessive fluid intake

Hypotonia:

- High fat:muscle ratio

Lack of vomiting reflex:

- Vomiting should be viewed seriously
- Gastroparesis and constipation may occur after binge
- Bowel necrosis and stomach rupture have been reported

High pain threshold:

- Watch out for unreported injuries/fractures
- Beware abdominal pain
- Unexplained bruising

Abnormal temperature control:

- Slight pyrexia must be viewed seriously

Hypogonadism:

- 5 reports worldwide of pregnancy, none of paternity

Intellectual ability:

- Range 50-100, with most in 60-65 region
- Delayed social/emotional skills
- Challenging behaviour

Capacity:

- The drive to eat overwhelms rational decision making
- Without supervision life-threatening amounts of food are consumed
- These characteristics are not uniform but occur over a spectrum.

Other features include:

- Obesity related problems;
- Obstructive sleep apnoea;
- Osteoporosis;
- Diabetes type 2;
- Oedema;
- Skin picking leading to cellulitis.

For further information, see following pages or visit www.pwsa.co.uk
PWSA UK Helpline: 01332 365676
Medical alerts in several languages are also available at
http://www.ipwso.org/#!medical-alerts-booklet/czxp

Further Information

Characteristics of Prader-Willi Syndrome (PWS)

PWS is a rare and complex genetic syndrome, first described in 1956, which affects people throughout their life. In about 95% of cases it is a *de novo* genetic abnormality affecting chromosome 15. There are probably no more than 2000 people with the syndrome throughout the UK. It is very rare for an adult with PWS to live totally independently; most still live with parents or relatives, or are in residential care or supported living. The range and severity of symptoms differs between individuals, but all will have the following characteristics in some degree:

Hyperphagia (overeating)

This is still not fully understood, but appears to stem from a dysfunction in the hypothalamus which means that the person does not know when they have had enough to eat - hence they feel hungry most of the time and act as someone who is starving. The desire to eat can overwhelm all rational decision-making processes with regard to food.

Hypotonia (low muscle tone) and abnormal body composition

The person is less active and needs fewer calories than another adult of the same age and height to maintain a healthy weight. Most individuals have a higher fat to muscle ratio than normal. As much as 50% of body weight is fat mass. It is thus advisable to start medications with a lower dose than normal.

Hypogonadism (immature sexual development)

Some people with PWS may have already experienced the first signs of sexual development as early as 5 years, with pubic and underarm hair appearing. However, in the majority of cases, full sexual development does not occur in either men or women with PWS. Women may not experience the onset of periods, or they may be very erratic, and breast development may be slow. Men's voice may not break and facial hair can be very scanty. Sex hormone treatment will help with these issues – specialist input from an endocrinologist is often helpful.

Whilst infertility is generally thought to be the norm, there have been five reports worldwide of women with PWS having a child (which, if the woman has the deletion form of PWS, has a 50-50 chance of being born with Angelman syndrome). There are no reports of a man with PWS fathering a child.

Short stature

Women average around 4' 9" (145 cm) in height and men around 5' 2" (158 cm). However, stature may be closer to that of other family members if the individual has received growth hormone as a child. A few individuals with PWS, however, even without growth hormone, are within normal height ranges.

Obesity

The combination of hyperphagia and hypotonia (especially when exacerbated by short stature) means that the person with PWS will become morbidly obese if external controls are not in place to prevent them accessing food. In addition, they usually require fewer calories per day than those without PWS to maintain a healthy weight.

Life expectancy
Early death as a result of morbid obesity is not uncommon, and has occurred in children and young adults. However, with restricted access to food, the person can live well into middle age and beyond. The oldest known person with PWS died at age 74 - she had lived in an institution for the greater part of her life.

Intellectual abilities
Intellectual abilities range from 50 to over 100. The majority are in the 60-65 range.

Immature or delayed social and emotional skills and challenging behaviour
Most people with PWS operate at a lower social and emotional level than their chronological age and intellectual level, sometimes displaying behaviours which can be seen in young children (eg temper outbursts) and refusal to comply with requests. Some can appear very able on first meeting, but this often masks difficulties in understanding.

Various cognitive deficits
Including:

- problems with attention-switching, resulting in oppositional behaviour and resistance to change
- problems with auditory processing - find it difficult to carry out instructions given verbally
- perseverative speech

Mental Capacity
Although a person with PWS may have the capacity to make decisions about many things, their capacity around food, money and health can be questioned, and a two part argument for lack of capacity can be put forward:

Q: Does the person with PWS have impairment of brain or mind?
A: Yes, even if they do not have an intellectual learning disability. Brain scans done under research conditions show definite impairment in the brain of people with PWS - ie messages from the stomach to the brain that they have had enough to eat are not getting through. A diagnosis of PWS automatically allows this argument to be put forward.

Q: Can the person make a reasoned decision about whether or not to eat?
A: No, the drive to eat overwhelms the rational decision-making process. Also the more "chaotic" the environment is, the more capacity to make decisions is decreased in PWS (ie they find it difficult to switch attention from one option or stimulus to another).

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Health care for people with PWS – unusual features
People with PWS are generally as healthy as the general population, and are also prone to the same illnesses and diseases. However there are some unusual features of PWS which require special attention and may not always be evident to those who have little experience of the syndrome. The following is a list of those features. Please note that they vary in degree between individuals with PWS and not all people with PWS will necessarily have all the features.

High pain threshold
Individuals with PWS frequently have decreased sensitivity to pain. Therefore, known injuries must be assessed for more serious problems, and signs of unreported injuries should be sought. In the absence of a verbal complaint of pain, other symptoms of specific injuries should be evaluated.

Bruising
Many individuals with PWS bruise easily but, because of the high pain threshold, are often unable to say how they came by the bruise.

Lack of vomiting reflex
Probably due to low muscle tone. If someone with PWS has a history of rare vomiting and presents with this symptom, it should be taken very seriously (see **food foraging** and **abdominal pain** below)

Abnormal temperature regulation
An individual with PWS may not be pyrexial even when seriously ill and may run dramatically below-normal temperatures at times. Even slight temperature elevations should be considered a warning sign. It is advisable to keep a record of the person's temperature when healthy, as this is sometimes below the normal average.

Food foraging
If left unsupervised, an individual with PWS may consume life-threatening amounts of food. A dramatic weight increase within a day - especially if coupled with reports of stomach distress or vomiting - may be a sign that the person is severely ill. Loss of appetite can also be a sign of illness. Stomach rupture is possible. Diarrhoea or significant fluid retention are also reasons for concern.
People with PWS can be quite indiscriminate in what they eat, eg poisonous berries, out-of-date food, frozen food, food from waste bins or off the ground. There are reports of people with PWS eating large quantities of items like salt or shampoo, though this is not thought to be very common. The lack of vomiting reflex (see above) may not alert the observer to the fact that the person has ingested items such as these.

Excessive fluid intake
There have been a few reports of people with PWS drinking excessive amounts of fluid, leading to potentially fatal low sodium and potassium levels.

Loss of appetite
Most people with PWS will continue to eat during illness and do not seem to experience the same loss of appetite as others might. A report of loss of appetite may be an indication of a serious illness. However, this should not be confused with a refusal to eat as a result of challenging behaviour.

Skin-picking
Skin picking or spot picking is very common in PWS. Skin picking is often provoked by small spots and grazes, which are picked continually, and thus never allowed to heal. However, sometimes wounds are made where there was no wound previously. Any area of the body can be a target. Most common are the limbs and the head or face, but other areas may be involved. Some people with PWS have been found to indulge in picking at

their rectums and genitals, and this should always be considered first if there are any rectal or genital problems occurring. Variations of this skin picking behaviour include pulling out hair, finger nails and toe nails. There is an increased risk of infection as a result.

Undetected bone fractures

Due to the high pain threshold, it is not unusual for a person with PWS to have an undetected broken bone. Following a fall or other injury, a person with PWS should be closely monitored for a change in walking or arm movement. Observe for deformities, swelling or bruising. In addition osteoporosis ('thin bones') is more common (because of the hypotonia and lack of sex hormones) and therefore a fracture may result from relatively minor trauma.

Abdominal pain

Individuals with PWS do not commonly exhibit a vomiting reflex. If a person with PWS suddenly reports abdominal pain or bloating, is vomiting, or has abdominal distention, there may be life-threatening bowel inflammation or necrosis, and emergency surgery may be needed. It also may be a warning that the person has ingested a large amount of food. In either case, death can occur in hours.
Recent reports have highlighted deaths due to "binge-eating", especially when the person with PWS usually has their food intake well-controlled and does not have a significant weight problem.

Gastroparesis and constipation

This is a condition that is common with PWS and can be more life threatening then in a typical situation. A person with Prader-Willi syndrome when diagnosed with gastroparesis may need hospitalization. People with PWS also commonly present with constipation, probably due to low muscle tone in the digestive tract.

Risk of choking

There is a risk of choking arising from people with PWS trying to eat food quickly, either because they habitually do this, or because they are trying to disguise the fact that they have taken food to eat which they should not have done. There have been reports of deaths in adults with PWS from this cause.

Obesity-related problems

High blood pressure, diabetes, oedema, congestive heart failure and respiratory failure are the most common problems for the adult who is significantly overweight.

Obstructive and central sleep apnoea

Sleep apnoea is relatively common and but may also occur in those who are not seriously overweight. Sleep checks are advisable every few years.

Risk from pneumonia

People with PWS may be more liable than the general population to pneumonia, which can have a very sudden onset and sometimes prove fatal. Adults should be offered a pneumonia vaccination.

Oedema and lymphoedema

Swelling of the legs and feet are common in PWS, especially in those who are overweight. However it can also occur in those who are not significantly overweight. There is a heightened risk of cellulitis.

Cortisol hormone insufficiency

There has been a suggestion that some people with PWS may be at increased risk of stress hormone (cortisol) deficiency due to hypothalamic problems but this has not been found in all studies and probably occurs only rarely. If there is a clinical suspicion of cortisol deficiency during an acute illness such as an infection (e.g. low blood sugar, low and variable blood pressure), then consideration should be made to urgently measure cortisol levels and if there is concern hydrocortisone could be administered until the results are available.

Anaesthesia

There is nothing inherent in PWS which gives cause for concern with the administration of anaesthesia. However, individual health problems related to PWS should be taken into account. These include:

- obesity (complications caused by obstructive apnoea, pulmonary hypertension, altered blood oxygen or blood carbon dioxide levels, significant oedema).
- high pain threshold (see above)
- temperature instability - parent or carer should be asked for information about patient's usual temperature
- thick saliva - may complicate airway management
- food seeking behaviours - the person may have eaten food even if they say they have not. Unless carer or parent can verify this, the person should be assumed to have food in their stomach.
- hypotonia may cause difficulties in ability to cough and clear airways
- excessive post-operative drowsiness in some individuals.

For more information, see
https://www.orpha.net/data/patho/Pro/en/Prader_Willi_EN.pdf

Mental health problems

Some people with PWS may also experience mental health problems. Researchers have found that those with the disomy type of PWS are more liable to these problems, although they can still be found in those with the deletion type. These can include: depression, lethargy, hallucinations and hearing voices, and acute psychotic episodes.

Annual health checks for people with PWS – additional checks

Prader-Willi Syndrome has a number of characteristics and potential health problems which may not be included within the framework of a standard annual health check for people with learning disabilities, as recommended in the government document "Valuing People Now". These are:

- Sleep apnoea (obstructive, central or mixed) - even where obesity is not a problem
- Scoliosis, kyphosis
- Osteoporosis (in both males and females, at young age, due to lack of sex hormones)

- Oedema
- Cellulitis
- Hypothyroidism
- Gastroparesis
- Diabetes (type 2)
- Skin infections (due to skin-picking)
- Vitamin D deficiency