BE ALERT
PRADER-WILLI SYNDROME (PWS)

Important Medical Alerts and Complications in this rare, genetic condition

An essential Guide for families, medical and healthcare professionals
About Consensus Gretton

Consensus Gretton is an acknowledged specialist provider of support and accommodation for adults with Prader-Willi Syndrome (PWS) with homes in Northamptonshire, Cambridgeshire, Stirlingshire and Essex.

Established in 1982, we have an in-depth understanding of this rare, genetic condition and a reputation for providing a high standard and best practice in PWS support. Health and well-being of the people we support is our utmost priority. We are passionate about broadening the understanding of PWS, working collaboratively with the NHS and A&E to raise awareness of the severe medical complications which can develop rapidly for individuals with PWS.

About this Guide

This guide was written by medical specialists in PWS on behalf of the Prader-Willi Syndrome Association in the USA (PWSA USA) - a charitable organisation supporting those living with PWS, their families and carers and professionals. It outlines the key medical alerts to be aware of and is a crucial companion ...

• For families and support workers supporting people daily with PWS to recognise symptoms and refer to at medical appointments
• For medical and healthcare professionals to understand why and how symptoms are presenting and act quickly in routine or emergency situations.

See our quick reference poster at the back of this guide for features of PWS requiring particular attention

“There is increased risk of respiratory difficulties including weak chest muscles, and sleep apnoea”

“Body temperature abnormalities may mean that fever may be absent despite serious infection”
Prader-Willi Syndrome (PWS) is a complex neurobehavioural genetic disorder resulting from an abnormality on the 15th chromosome. It occurs in males and females and equally in all races.

PWS typically causes low muscle tone, short stature if not treated with growth hormone, cognitive deficits, incomplete sexual development, problem behaviours, and a chronic feeling of hunger that, coupled with a metabolism that utilises drastically fewer calories than normal, can lead to excessive eating and life-threatening obesity.

At birth the infant has a low birth weight for gestation, hypotonia, and difficulty sucking due to weak muscles (“Failure to thrive”). The second stage (“Thriving too well”), with onset between the ages of two and five throughout lifetime, may show increased appetite, weight control issues, and motor development delays along with behaviour problems.

Other factors that may cause difficulties include negative reactions to medications, high pain tolerance, gastro-intestinal and respiratory issues, lack of vomiting, and unstable temperature.

Severe medical complications can develop rapidly in individuals with PWS.

“Awareness of why symptoms are presenting is vital and could save someone’s life”
Medical Alert
Important Considerations
For Routine Or Emergency Treatment
Medical professionals can contact the PWSA (UK) to obtain more information; they may put
you in touch with a specialist as needed.

Anaesthesia, medication reactions
People with PWS may have unusual reactions
to standard dosages of medications and
anaesthetic agents. Use extreme caution in giving
medications that may cause sedation; prolonged
and exaggerated responses have been reported.

Anesthesia and PWS:
James Loker, MD, Laurence Rosenfield, MD
www.pwsausa.org/medical-issues-a-z/ and view
the medical section for articles on Anesthesia.

Adverse reactions to
some medications
People with PWS may have unusual reactions to
standard dosages of medications. Use extreme
cautions in giving medications that may cause
sedation; prolonged and exaggerated responses
have been reported. Water intoxication has
occurred in relation to use of certain medications
with anti-diuretic effects, as well as from excess
fluid intake alone.

Water intoxication
www.pwsausa.org/medical-issues-a-z/
and view the Medical section for articles on
Water intoxication.

High pain threshold
Lack of typical pain signals is common and may
mask the presence of infection or injury. Someone
with PWS may not complain of pain until infection
is severe or may have difficulty localising pain.
Parent/caregiver reports of subtle changes in
condition or behaviour should be investigated for
medical cause.

Respiratory concerns
Individuals with PWS may be at increased risk
of respiratory difficulties. Hypotonia, weak chest
muscles, and sleep apnoea are among possible
complicating factors. Anyone with significant
snoring, regardless of age, should have a medical
evaluation to look for obstructive sleep apnoea.

Recommendations for Evaluation of Breathing
Abnormalities Associated with Sleep in Prader-
Willi Syndrome
PWSA (USA) Clinical Advisory Board
Consensus Statement 12/2003
www.pwsausa.org/medical-issues-a-z/
and view the medical section for articles on
Breathing Issues
*All the information found at this website on Evaluation of
Breathing is printed in its entirety in this “Medical Alerts”
book (page 4).

Other problems
Other problems that can cause respiratory
difficulties in the young can be chronic
stomach reflux and aspiration. Although the
lack of vomiting is felt to be prominent in PWS,
reflux has been documented and should be
investigated in young children with chronic
respiratory problems. Individuals with obstructive
apnoea are at more risk for reflux as well.

Respiratory Problems in PWS:
James Loker, MD
www.pwsausa.org/medical-issues-a-z/
and view the medical section for articles on
Breathing Issues
Lack of vomiting
Vomiting rarely occurs in those with PWS. Repeated induced vomiting may be ineffective and may cause toxicity. This characteristic is of particular concern in light of hyperphagia and the possible ingestion of uncooked and spoiled, or otherwise harmful food items. The presence of vomiting may signal a life-threatening illness.

Severe gastric illness (GI problems)
Abdominal distention or bloating, pain, and/or vomiting may be signs of life-threatening gastric inflammation or necrosis, more common in PWS than in the general population.

Rather than localised pain, there may be a general feeling of being unwell. A condition described as acute idiopathic dilation has been reported. In this condition, a person with PWS greatly distends their stomach with food, (slimmer people may be more at risk) and does not get the normal message of fullness or pain. They may distend their stomach to the point of cutting off the blood supply causing necrosis. Another risk of binge eating that can create a serious medical emergency is GI perforation. If an individual with PWS has these symptoms, close observation is needed. An X-ray, CT scan or ultrasound may help in differentiation.

This should be considered a surgical emergency and exploratory laparotomy may be life saving.

In addition, severe stomach pain may be caused by gallstones or pancreatitis. An ultrasound, chemistry analysis of the blood and CT of the abdomen will help with the diagnosis.

Medical Alert: Stomach Problems Can Signal Serious Illness
www.pwsusa.org/medical-issues-a-z/
and view the medical section for articles on GI Problems - Stomach/Intestines

Gastroparesis
Another consideration is Gastroparesis, a weakness of the stomach. This is a condition that is common with PWS and can be more life threatening than in a typical situation. A child with PWS, when diagnosed with Gastroparesis, may need hospitalisation. Eating while the stomach is distended with Gastroparesis can be very dangerous. For more information go to: www.gicare.com/diseases/gastroparesis/

Body temperature abnormalities
Idiopathic hyper- and hypothermia have been reported. Hyperthermia may occur during minor illness and in procedures requiring anaesthesia. Fever may be absent despite serious infection.

Skin lesions and bruises
Because of a habit that is common in PWS, open sores caused by skin picking may be apparent. Individuals with PWS also tend to bruise easily. Appearance of such wounds and bruises may wrongly lead to suspicion of physical abuse.

Hyperphagia (excessive appetite)
Insatiable appetite may lead to life-threatening weight gain, which can be very rapid and occur even on a low-calorie diet. Individuals with PWS must be supervised at all times in all settings where food is accessible. Those who have normal weight have achieved this because of strict external control of their diet and food intake.

1 Wharton RH et al. (1997) Acute idiopathic gastric dilation with gastric necrosis in individuals with PWS. American Journal of Medical Genetics, Dec. 31;Vol. 73(4): page 437-441
Surgical and Orthopaedic concerns

In view of the increasing number of infants and children with PWS undergoing sleep assessments prior to growth hormone treatment and the potential rise in surgical procedures (e.g., tonsillectomy) requiring intubation and anaesthesia, it will be important to alert the medical team about complications. These complications may include trauma to the airway, oropharynx, or lungs due to possible anatomic and physiologic differences seen in PWS such as a narrow airway, underdevelopment of the larynx and trachea, hypotonia, oedema, and scoliosis.

Musculoskeletal manifestations including scoliosis, hip dysplasia, fractured bones and lower limb alignment abnormalities are described in the orthopaedic literature. However, care of this patient population from the orthopaedic surgeon’s perspective is complicated by other clinical manifestations of PWS.

PWS: Clinical Concerns for the Orthopedic Surgeon

Martin J. Herman, MD, Department of Orthopedic Surgery, St. Christoper’s Hospital for Children www.pwsausa.org/medical-issues-a-z/ and view the medical section for articles on Orthopedic Issues

Recommendations for Evaluation of Breathing Abnormalities Associated with Sleep in PWS

PWSA (USA) Clinical Advisory Board Consensus Statement - 12/2003

Problems with sleep and sleep disordered breathing have been long known to affect individuals with PWS. The problems have been frequently diagnosed as sleep apnoea (obstructive [OSA], central or mixed) or hypoventilation with hypoxia. Disturbances in sleep architecture (delayed sleep onset, frequent arousals and increased time of wakefulness after sleep onset) are also frequently common. Although prior studies have shown that many patients with PWS have relatively mild abnormalities in ventilation during sleep, it has been known for some time that certain individuals may experience severe obstructive events that may be unpredictable.

Factors that seem to increase the risk of sleep disordered breathing include young age, severe hypotonia, narrow airway, morbid obesity and prior respiratory problems requiring intervention such as respiratory failure, reactive airway disease and hypoventilation with hypoxia. Due to a few recent fatalities reported in individuals with PWS who were on growth hormone therapy* (GH) some physicians have also added this as an additional risk factor. One possibility (that is currently unproven) is that GH could increase the growth of lymphoid tissue in the airway thus worsening already existing hypoventilation or OSA. Nonetheless, it must be emphasised that there are currently no definitive data demonstrating GH causes or worsens sleep disordered breathing. However, to address this new concern, as well as the historically well documented increased risk of sleep-related breathing abnormalities in PWS, the Clinical Advisory Board of the PWSA (USA) makes the following recommendations:

*Reported by PWSA USA
1. A sleep study or a polysomnogram that includes measurement of oxygen saturation and carbon dioxide for evaluation of hypoventilation, upper airway obstruction, obstructive sleep apnoea and central apnoea should be contemplated for all individuals with PWS. These studies should include sleep staging and be evaluated by experts with sufficient expertise for the age of the patient being studied.

2. Risk factors that should be considered to expedite the scheduling of a sleep study should include:

- Severe obesity - weight over 200% of ideal body weight (IBW).
- History of chronic respiratory infections or reactive airway disease (asthma).
- History of snoring, sleep apnoea or frequent awakenings from sleep.
- History of excessive daytime sleepiness, especially if this is getting worse.
- Before major surgery including tonsillectomy and adenoidectomy.
- Prior to sedation for procedures, imaging scans and dental work.
- Prior to starting growth hormone or if currently receiving growth hormone therapy.

Additional sleep studies should be considered if patients have the onset of one of these risk factors, especially a sudden increase in weight or change in exercise tolerance. If a patient is being treated with growth hormone, it is not necessary to stop the growth hormone before obtaining a sleep study unless there has been a new onset of significant respiratory problems.

Any abnormalities in sleep studies should be discussed with the ordering physician and a pulmonary specialist knowledgeable about treating sleep disturbances to ensure that a detailed plan for treatment and management is made. Referral to a paediatric or adult pulmonologist with experience in treating sleep apnoea is strongly encouraged for management of the respiratory care. In addition to a calorie restricted diet to ensure weight loss or maintenance of an appropriate weight, a management plan may include modalities such as:

- Supplemental oxygen.
- Continuous positive airway pressure (CPAP) or BiPAP.
- Oxygen should be used with care as some individuals may have hypoxemia as their only ventilatory drive and oxygen therapy may actually worsen their breathing at night.
- Behaviour training is sometimes needed to gain acceptance of CPAP or BiPAP.
- Medications to treat behaviour may be required to ensure adherence to the treatment plan.

If sleep studies are abnormal in the morbidly obese child or adult (IBW > 200%) the primary problem of weight should be addressed with an intensive intervention - specifically, an increase in exercise and dietary restriction. Both are far preferable to surgical interventions of all kinds. Advice for achieving this is available from the PWSA (UK) and Gretton Homes. Behavioural problems interfering with diet and exercise may need to be addressed simultaneously by persons experienced with PWS.

If airway related surgery is considered, the treating surgeon and anaesthesiologist should be knowledgeable about the unique pre- and post operative problems found in individuals affected by PWS.

Anesthesia and PWS
James Loker, MD, Laurence Rosenfield, MD
www.pwsausa.org/medical-issues-a-z/ and view the medical section for articles on Anesthesia
Tracheostomy surgery and management presents unique problems for people with PWS and should be avoided in all but the most extreme cases. Tracheostomy is typically not warranted in the compromised, morbidly obese individual because the fundamental defect is virtually always hypoventilation, not obstruction. Self endangerment and injury to the site are common in individuals with PWS who have tracheostomies placed.

At this time there is no direct evidence of a causative link between growth hormone and the respiratory problems seen in PWS. Growth hormone has been shown to have many beneficial effects in most individuals with PWS including improvement in the respiratory system. Decisions in the management of abnormal sleep studies should include a risk/benefit ratio of growth hormone therapy. It may be reassuring for the family and the treating physician to obtain a sleep study prior to the initiation of growth hormone therapy and after 6-8 weeks of therapy to assess the difference that growth hormone therapy may make. A follow up study after one year of treatment with growth hormone may also be indicated.

*All the information found at this website is printed in its entirety on pages 6-10

**Anaesthesia and Prader-Willi Syndrome**

James Loker, MD, Laurence Rosenfield, MD

**Issues Affecting PWS and Anaesthesia In individuals with PWS there are health issues that can alter the course of anaesthesia**

**Obesity** - Obese individuals are more prone to obstructive apnoea, pulmonary compromise and diabetes. Each of these should be taken into account when preparing for anaesthesia. The individual may have altered blood oxygen or blood carbon dioxide levels that will change their response to medications including oxygen. Pulmonary hypertension, right-heart failure, and oedema may necessitate evaluation by a cardiologist or pulmonologist prior to surgery. An ECG to detect right ventricular hypertrophy may be beneficial to assess pulmonary hypertension. Frequently obese individuals with PWS may have significant body oedema (extra fluid) that is not fully appreciated due to obesity. This should be carefully evaluated, and if necessary, diuretics used before and after the anaesthesia. Airway management can be a particular problem when conscious sedation is used.

**High Pain Threshold** - Individuals with PWS may not respond to pain in the same manner as others. While this may be helpful in post-operative management, it may also mask underlying problems. Pain is the body’s way of alerting us to problems. After surgery, pain that is out of proportion to the procedure may alert the physician that something else is wrong. Other possible signs of underlying problems should be monitored.

**Temperature Instability** - The hypothalamus regulates the body’s temperature. Because of a disorder in the hypothalamus, individuals with PWS may be either hypo- or hyperthermic. The parent or caregiver can be helpful in letting the anaesthesiologist know what the individual’s usual temperature is. Although there is no indication of a predisposition to malignant hyperthermia in PWS, depolarising muscle relaxants (i.e. succinylcholine) should be avoided unless absolutely necessary.

**Thick Saliva** - A common problem in PWS is unusually thick saliva. This can complicate airway management, especially in cases of conscious sedation or during extubation (when a breathing tube is removed). Thick saliva also predisposes an individual to dental caries (cavities) and loose teeth. Oral hygiene should be evaluated prior to anaesthesia.
Food-Seeking Behaviours - It is vitally important that any individual undergoing general anaesthesia or conscious sedation have an empty stomach. This reduces the risk of aspiration of the stomach contents into the lungs. Individuals with PWS generally have an excessive appetite and may not tell the truth if they have eaten just prior to surgery. Any individual with PWS should be assumed to have food in the stomach unless it is verified by the caregiver that they have not eaten. A tube may need to be placed in the stomach to assure no food is present prior to attempting to place the breathing tube. Some individuals with PWS may ruminate (regurgitate some of their food) and are at higher risk of aspiration.

Hypotonia - The majority of infants with PWS are significantly hypotonic. This usually improves by 2-4 years of age. The majority, however, continue to have lower muscle tone than normal individuals. This may be a problem in the ability to cough effectively and clear the airways after use of a breathing tube.

Skin Picking - Habitual skin picking can be a significant problem in PWS. This can complicate healing of intravenous (IV) sites and incisional wounds. Usually if these remain well covered, they will be left alone.

Hypothyroidism - Since PWS is a hypothalamic disorder, other hypothalamic functions are at risk. Although the incidence of hypothyroidism in PWS is not known, low levels of thyroid hormone could occur due to lack of thyroid stimulating hormone or thyroid releasing factor, not necessarily due to problems of the thyroid gland itself. A check of thyroid hormone levels may be beneficial in the preoperative evaluation.

Difficult IV Access - Due to several problems including obesity and lack of muscle mass, individuals with PWS may pose difficulties with insertion of an intravenous line. A stable IV line should be present in any individual undergoing anaesthesia.

Behaviour Problems - Individuals with PWS are more prone to emotional outbursts, obsessive-compulsive behaviours, and psychosis. They may be on extensive psychotropic medication, and the possible interaction of these medicines with anaesthesia should be appreciated.

Growth Hormone Deficiency - All individuals with PWS should be considered growth hormone deficient. Growth hormone deficiency does not appear to alter cortisol release in response to stress; so steroid supplementation is not necessary. Individuals with PWS who are not on growth hormone treatment may have smaller airways than would be expected for their body size.

Recovery Post Anaesthesia
Drowsiness after anaesthesia may be due to the underlying somnolence and a component of central apnoea. For typical outpatient procedures, consideration should be given to an overnight observation. As mentioned above, a majority of the problems are due to obesity, central and obstructive apnoea, but weak muscle tone and chronic aspiration may also play a role in post anaesthesia respiratory issues.

Summary
Individuals with PWS can safely undergo anaesthesia. Risks are related to their general health before the procedure. The majority of complications do not appear to come from general anaesthesia, which is always closely monitored, but from poorly monitored conscious sedation. Only a physician familiar with the patient and their individual medical needs should make valid medical decisions.
**Summary:** PWS is a genetic disorder with documented patterns of health challenges and many hypothalamic related medical concerns

- Hyperphagia – excessive appetite from about the age of 2 but sometimes later
- Hypotonia – weak muscle tone especially in infancy
- Hypogonadism – most require hormone replacement
- Typically short stature and often growth hormone deficient
- Learning disability ranging from mild to severe
- Emotional problems including temper outbursts, anxiety and stubbornness

Due to the hypothalamic dysfunction, there is poor body temperature regulation, high pain threshold and, with the additional lack of vomiting, a person with PWS can have a serious medical problem which may remain overlooked.

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**Features of PWS requiring particular attention**

### Vomiting/Abdominal Pain

People with PWS do not normally vomit. When pain, flatulence, abdominal distension and vomiting are present, this could be life threatening. It may also be a sign that a large amount of food has been consumed, which can also be life threatening.

### Food Foraging

If unsupervised, some people with PWS may consume life threatening amounts of food including out of date or frozen food. Abdominal pains and or vomiting may be a sign that a person is seriously ill. Stomach rupture is possible. Diarrhoea or significant fluid retention can also signal emergency GI issues.

### Temperature

An individual with PWS may not present with a fever even when seriously ill and may run dramatically below normal temperature at times. Even slight temperatures should be considered a warning sign when looking at other symptoms and signs of ill health.

### High Pain Threshold & Bruising

People with PWS often have decreased sensitivity to pain. They may also bruise easily, common in PWS with no obvious explanation. Reported injuries must be assessed and closely observed for more serious problems.

Where pain is not reported, observe for other signs of injury eg bruising, swelling or bone fractures. Do not expect the person with PWS to necessarily complain of pain whether ill or injured.

### Mental Health Problems

Some teenagers and adults with PWS may also experience mental health problems. These can include depression, lethargy, hallucinations and hearing voices and acute psychotic episodes, often with a rapid onset.

### Respiratory Problems

Obstructive Sleep Apnoea

Excessive weight together with poor muscle tone (common in PWS) can lead to serious respiratory problems. Sleep apnea is common.

Obesity Related Problems

High blood pressure, diabetes, congestive heart failure and respiratory failure are the most common problems for the person with PWS who is overweight. Pulmonary embolism should be considered in anyone presenting with sudden cardiovascular compromise.

### Excessive Fluid Intake

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

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Consensus Gretton would like to thank PWSA (USA) for their help in producing this booklet. www.pwsausa.org

Consensus Gretton is part of Consensus who support over 500 adults and young people with learning disabilities, autism and complex needs.