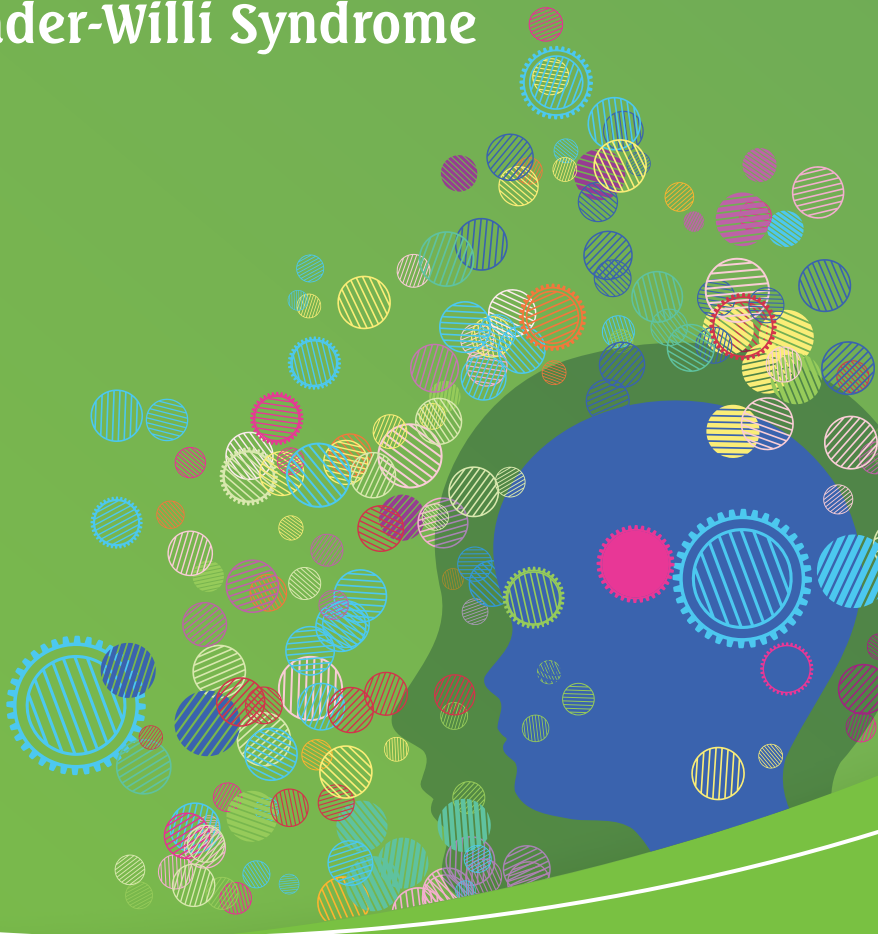
Hormones and Me

Prader-Willi Syndrome



ANZSPED
AUSTRALIA AND NEW ZEALAND
SOCIETY FOR PAEDIATRIC
ENDOCRINOLOGY AND DIABETES

Table of Contents

About this Book

This booklet is for the families of children with Prader-Willi syndrome (PWS) and for others who are important in their lives.

The booklet explains how Prader-Willi syndrome affects people. It gives information about commonly used medications, therapies, care, and supports. Early intervention and hormonal therapies have greatly improved outcomes for children with PWS in recent years. This booklet is designed to inform you about how to understand PWS so that you and your family can be confident and knowledgeable in decision-making and management.

There are headings to help you find your way. Not everything in the booklet will be relevant to every person with PWS. A glossary at the back of the booklet defines all technical terms.

The booklet was co-authored by caregivers of children with PWS, health professionals, and researchers with specialist knowledge about PWS: A. Marie Blackmore and Jenny Downs (Telethon Kids Institute, Nedlands, WA, Australia), Yoon Hi Cho (The Children's Hospital at Westmead, Sydney, NSW, Australia), Patricia Crock (John Hunter Children's Hospital, Newcastle, NSW, Australia), Gillian M. Nixon (Monash Children's Hospital, Clayton, VIC, Australia), Lauren Rice (The University of Sydney, NSW, Australia), Louise Clayton, Ros Catalano, Katherine Garvey, and Kerry Saddler (parents of children with PWS), and Jacqueline A. Curran, Rebecca Flavel, and Catherine S. Choong (Perth Children's Hospital, Nedlands, WA, Australia). We gratefully acknowledge the contributions of Dr Elaine Tham (Women's and Children's Hospital, North Adelaide, SA, Australia) and Dr Peter Simm (Royal Children's Hospital, Melbourne, Australia) who reviewed the booklet and Ms Gillian Northcott (Perth Children's Hospital, Nedlands, WA, Australia) who did the illustrations in this booklet.

Merck is proud to bring you this booklet from the Hormones and Me educational series. We hope that you find it a valuable and helpful resource.

This booklet was supported by the Australia and New Zealand Society for Paediatric Endocrinology and Diabetes (ANZSPED) council with a ANZSPED grant.

List of Abbreviations

ACTH
Adrenocorticotropic Hormone

ASD
Autism Spectrum Disorder

CSA
Central sleep apnoea

FISH
Fluorescence in-situ hybridization test

GH
Growth hormone

mUPD
Maternal uniparental disomy

OSA
Obstructive sleep apnoea

PWS
Prader-Willi syndrome

TSH
Thyroid Stimulating Hormone

Introduction

Prader-Willi syndrome (PWS) is a genetic condition that people are born with. It affects similar numbers of boys and girls. There are some big challenges with PWS, but it's important to know that people with PWS can lead full, active, and happy lives. They love and are loved by their families and friends; they go to school, do both paid and voluntary work (usually part-time), actively engage in many community activities (e.g., swimming, horse riding, team sports), and have their own hobbies and interests like everyone else. But they need extra supports and some medications and other medical treatments to help them to achieve this quality of life. A lot is known nowadays about what is needed and there are many options available to families of children with PWS.

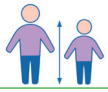
PWS is caused by genetic changes inside the body's cells. Our genetic material programs the way our bodies develop, from the colour of our hair to the way we grow and develop. The genetic changes that cause PWS can affect many different body functions. The main changes are summarised in *Diagram 1*. PWS is highly variable, so not every child with PWS will have all of these conditions. If they do have difficulties in an area, some will have only mild problems while others will have more severe problems.

Every child with PWS is different. Each child's caregivers will become the experts on their child's health issues. The more you can find out about PWS, the better decisions you can make for your child. This booklet is designed to help you to do that. It provides evidenced-based information about the health, growth, and development of children with PWS and some treatments for this condition.

This booklet is also designed to point you in directions where you can find more specific help and supports for your child's needs. There are

many healthcare professionals with specialist knowledge about children with PWS including paediatric endocrinologists, paediatricians, speech pathologists, clinical psychologists, dietitians. There are parent support groups. And there are opportunities to participate in research studies to find out more about ways to support children with PWS and their families.

Diagram 1: Children with PWS may have:

	Slow growth and short stature.
	Interest in food, insatiable appetite, and excessive eating (starting early to mid-childhood) with a tendency to become overweight, unless closely supervised.
	Sleep apnoea and daytime sleepiness.
	Weak floppy muscles (low muscle tone), especially when an infant. This may improve during childhood.
	Chest and breathing problems, including sleep apnoea and tendency to chest infections.
	A friendly, caring personality that can have sudden meltdowns that are difficult to control.
	Slow sexual development: small genital organs; low fertility or infertility.
	Certain challenges with thinking and learning. This can include challenges learning some school lessons, challenges understanding conventions of social interactions, and challenges tolerating unexpected changes in routine.
	Delayed motor milestones and a tendency to be less physically active.

Genetics

PWS is caused by changes to certain genes. Genetic testing to diagnose PWS is done using a blood test, usually in the early weeks after birth.

Each person's genetic material is made up of 23 pairs of chromosomes. One chromosome from each pair is inherited from each parent. So normally, people inherit one copy of chromosome 15 from their father (called the paternal copy) and one copy of chromosome 15 from their mother (called the maternal copy).

PWS is a genetic disorder caused by changes to genes in a particular area of chromosome 15 (the 15q11-q13 region). It is very rare: only about 1 in 16,000 babies are born with PWS. PWS was first described in 1956 by Swiss doctors (Andrea Prader, Alexis Labhart, and Heinrich Willi). In PWS, changes to chromosome 15 can happen in one of four ways, as shown in *Table 1*.

In over 90% of people with PWS, it is caused by a once-off (sporadic) genetic change. In this case, there is no family history of PWS and extremely low risk of PWS in other children born to the same parents. However, if the PWS was caused by a micro-deletion, there is a 50% chance that other children of the same parents will be born with PWS. If the PWS was caused by a translocation, there is 10-25% chance that other children of the same parents will be born with PWS. It is important to discuss this with your clinician.

A doctor may recommend genetic testing if a baby has certain characteristics (e.g., reduced activity in the womb before birth, floppy

Table 1: Types of genetic changes that can cause PWS

	Genetic change	What happens to the genetic material
1	Paternal 15q11-q13 deletion	Most people with PWS (50–70%) inherit a chromosome 15 from their father where the 15q11-q13 region is missing.
2	Maternal uniparental disomy (mUPD)	Some people with PWS (25–30%) inherit two copies of chromosome 15 from their mother and none from their father.
3	Imprinting defects	A few people with PWS (less than 3%) have other genetic changes to the 15q11-q13 region of chromosome 15. These include microdeletions (where a very small number genes are deleted) and epi-mutations (which affect the way the genes function).
4	Translocations	A very small number of people with PWS (less than 0.1%) have rearrangements of their chromosomes that involve the 15q11-q13 region of chromosome 15. A chromosome has broken and one part of it has attached to a different chromosome, which results in the gene not working properly.

muscles or difficulties sucking). Genetic testing for PWS uses a blood test and is usually done in the early weeks after birth.

A methylation test is a blood test that can detect any genetic type of PWS. If a methylation test shows that the baby has PWS, then more blood tests might be needed to work out exactly what type of genetic change the child has. If an imprinting defect seems likely, then both parents might be asked to have blood tests.

A FISH (fluorescence in-situ hybridization) test is a blood test that detects PWS only if it is by paternal 15q11-q13 deletion. This test doesn't detect the other types of PWS.

How the Hypothalamus Works

The hypothalamus is a part of the brain. It controls the endocrine system of the body, which manages many body functions, including hunger, growth, and sleep. When the hypothalamus gives wrong messages to the body, many different body functions are affected. This is what happens in PWS.

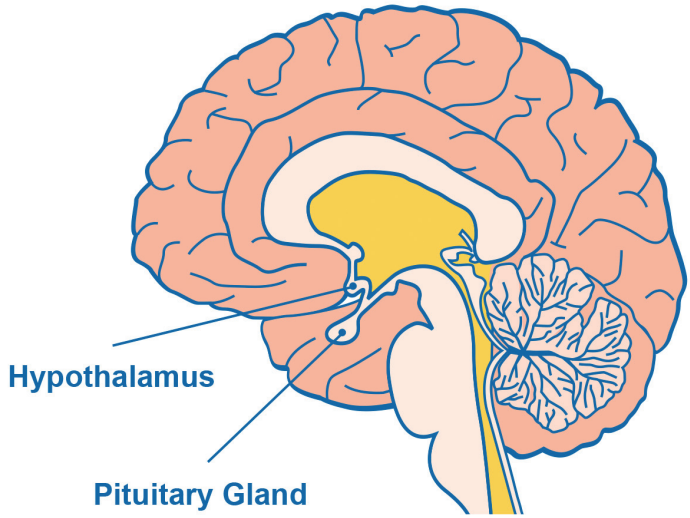
The genetic changes in PWS affect the way the hypothalamus works. The hypothalamus is a structure deep inside the brain. It receives messages from other parts of the body through the nervous system and sends hormones (chemical messengers) into the bloodstream to control many of the body's functions, including body temperature, hunger and thirst, growth, sexual functions, emotions and behaviour, and sleep.

The hypothalamus works very closely with the pituitary gland (which sits beneath the hypothalamus, as shown in *Diagram 2*). The hormones from the hypothalamus tell the pituitary gland to release hormones.

The hypothalamus and pituitary are parts of the endocrine system, a network of organs that release hormones into the bloodstream to regulate many body functions. Some of the other organs that are members of the endocrine system are shown in *Diagram 3 (see page 12)*. They are the thyroid and parathyroid (in the throat), the adrenal gland (on top of each kidney), the pancreas (behind the stomach), and the ovaries (in females) and testes (in males).

In PWS, the hypothalamus doesn't give the correct messages to other

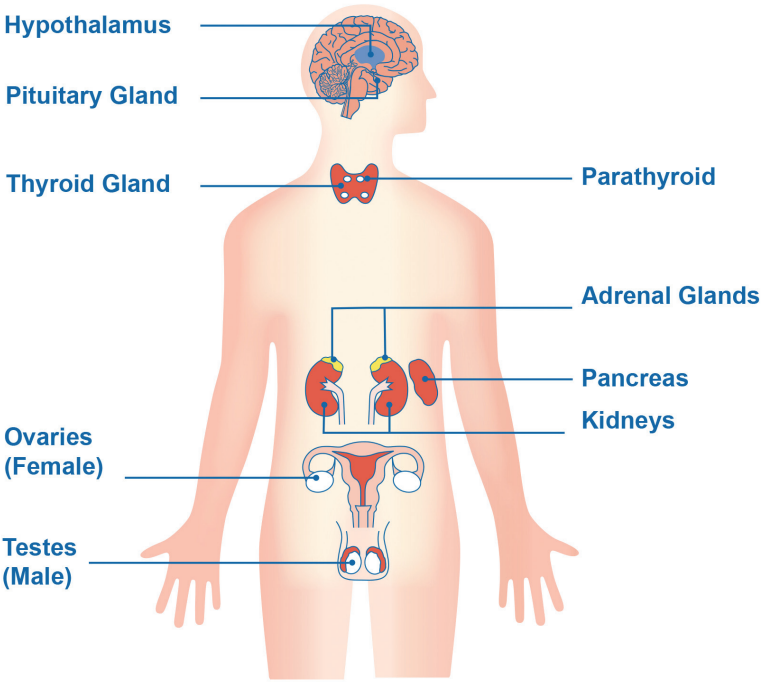
Diagram 2: Hypothalamus and pituitary gland



members of the endocrine system, so they don't produce the right amounts of hormones at the right time. The endocrine system affects many different body functions. Therefore, when the hypothalamus isn't working properly, many different body functions may be affected.

Endocrinologists are specialists in the endocrine system. They can explain how changes in hormone production can affect different body functions and what treatments are likely to help.

Diagram 3: Endocrine glands



Growth and Growth Hormone

People with PWS are shorter than average unless they take growth hormone (GH). Most children with PWS take GH, as it not only stimulates growth but also has other benefits.

Many, if not all, children with PWS secrete less growth hormone (GH) than other children, and so children with PWS may be short. Without GH treatment, the average height of men with PWS is 155cm and of women is 148cm. Lower levels of GH also has other effects: it causes low muscle tone, muscle weakness, less stamina, more fat tissue and less lean tissue in the body, and it slows down the chemical processes in the body.

Children with PWS may begin GH treatment during infancy or early childhood. Research studies show that GH treatment helps people with PWS to grow taller and reduces their body fat. GH has further health benefits in adult life (e.g., more lean tissue and less fat in the body, better quality of life, greater muscle strength, greater exercise capacity, and improved lung function).

GH treatment is generally safe for children with PWS. Specific precautions need to be considered before and during the early phase of treatment, based on a sleep study assessment and advice from a sleep physician and paediatric endocrinologist before starting GH therapy.

People with PWS are more likely to develop scoliosis as they grow than people without PWS. It isn't clear what role GH might have in developing scoliosis, but it is important to monitor children for scoliosis throughout their childhood and adolescence. There is a small risk of damage to the hip (slipped capital epiphyses) with GH therapy. Although accurate estimates are not available, these adverse side effects of GH therapy are very uncommon.

Body Weight and Eating

During childhood, many children with PWS develop an intense, insatiable hunger, which is not satisfied, even after eating. This can lead to excessive weight gain, unless properly managed. Several different treatments are available, including dietary management, physical activity, growth hormone, medications, and surgery. Several specialists can help in these areas, including endocrinologists, dietitians, physiotherapists, and exercise physiologists. Other families of children with PWS can also help to suggest strategies for controlling hunger and weight gain.

Body weight

People with PWS are prone to putting on weight. But whereas most people's excess fat accumulates around the waist, people with PWS have more fat in their arms and legs.

In all people, the more muscle there is, the greater the body's resting energy expenditure will be. People with PWS have less muscle and more fat than other people. Therefore, their resting energy expenditure is lower. This means that, even at rest, their bodies are burning up less energy than other people of the same body weight.

Early nutritional changes in PWS

Babies born with PWS have weak muscle tone and difficulty sucking. They often need feeding assistance to make sure they get enough

nutrition. These eating problems soon improve, and the growth of children with PWS is normal until about 2 years of age. After 2, children with PWS start to gain excess weight. After 4 years of age, their appetite may increase because their body doesn't give the right signals to show that they have had enough to eat.

Hyperphagia

From early to mid childhood, children with PWS often develop hyperphagia, which is an intense, insatiable desire for food. Even after eating a substantial meal, their body does not signal to their brain that they have had enough. This is due to hormone differences between people with and without PWS. For most people with PWS, hyperphagia is a lifelong problem. An adult with PWS says, "When I think of food, my eyes shine, and when I see food, I want it at all costs, and I cannot stop myself. I am always hungry, and I never get enough; when I overeat, I feel sick. When they tell me that I should not eat so much, I get angry and anxious."

Hyperphagia in PWS, if not well-managed, causes uncontrollable weight gain and extreme obesity. This can lead to metabolic syndrome, type 2 diabetes mellitus, sleep apnoea, respiratory insufficiency, and cardiovascular disease. In recent years, there have been huge improvements in managing body weight in PWS. A parent of a child with PWS advises other parents to "avoid frightening stories or really obese pictures on the Internet. Those are in older kids and adults that weren't diagnosed soon enough. Now we know what to do."

Managing hyperphagia

Various ways of managing hyperphagia have been trialled. The current evidence regarding these management strategies is summarized below, although more evidence is being generated all the time.

- **Dietary management:** This is the first line of management of hyperphagia and obesity in PWS. Children with PWS need only 60–80% of the calories that children without PWS need. An energy-restricted diet has been found beneficial, with high dietary fibre and low intake of high-kilojoule food and drinks. To avoid nutritional deficiencies, standard over-the-counter age-appropriate multivitamin supplementation is often advised. An experienced dietitian can create a balanced dietary plan.

- **Food security:** means the child has a clear, predictable meal schedule, and food is kept out of sight and out of mind at other times. This helps children with PWS stick to a defined food intake and control their weight, and it makes them less anxious about food. A dietitian can advise about this. See page 27 of this booklet for more about food security.

- **Physical Activity:** Programs that increase activity levels for children and adults with PWS can have several benefits, including fitness, muscle strength, body coordination, and, to some extent, weight loss. It is doubtful whether physical exercise alone could be used to control weight, but exercise is recommended for PWS alongside other management strategies for weight control. Experienced physiotherapists and exercise physiologists can help create a physical activity plan.

- **Growth hormone replacement therapy:** GH treatment reduces body fat and increases muscle mass in children and adults with PWS.

- **New medications:** Several new medications for hyperphagia and obesity are currently being trialled with children and adults with PWS. Some of these appear to reduce hyperphagia and body fat. Research trials are currently under way to make sure they are safe, well-tolerated, and effective.

- **Bariatric surgery:** Surgeries that reduce the size of the stomach are intended to make a person feel as though they have eaten enough after a smaller meal. This treatment is not currently recommended for people with PWS, because the evidence shows that although they lose weight at first, they don't maintain the weight loss in the long term.

In managing hyperphagia and obesity, the best results are when the person is managed by a multidisciplinary team including their paediatrician, dietitian, physical therapist, and endocrinologist from an early age to prevent early onset obesity.

As well as the previously listed treatments, families of children with PWS also develop their own individual strategies for dealing with food. A child with PWS said, "I do not think about food; I go for long walks; I do crossword puzzles and other puzzles; and I play on my tablet and computer." A parent said, "We tried to accustom the whole family to healthy eating as much as possible. I taught my son to read nutrition labels so that later he would be able to choose what is best. He already knows that he must not eat too much sugar and fat." An adult with PWS said, "If I am happy and motivated, I do not go looking for food."

Breathing and Sleep

Children with PWS often have breathing-related problems (apnoeas) during sleep. They may also get very sleepy during the daytime. Children with PWS are at risk of food, drink or saliva going down the wrong way (aspiration or choking) and they may have weak chest muscles and be vulnerable to chest infections. There are treatments for all these conditions, and respiratory and sleep physicians are specialists who can assist your child in these areas.

Children and adults with PWS often experience sleep-related problems at night and during the daytime. At night, there can be different types of problems with breathing. In the daytime, people with PWS may be excessively sleepy and this can affect their ability to concentrate, their behaviour, and their quality of life.

There are a number of ways of managing these sleep problems. Respiratory and sleep physicians can assess and treat any of the conditions described in this section.

Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) occurs when there is repetitive obstruction of the upper airway (nose and throat) during sleep. This obstruction makes it difficult or impossible for air to move in and out the lungs for a few seconds or up to a minute. This can result in low oxygen levels or the person may wake up repeatedly in the night and be unable to get a restful sleep. People with OSA snore or have noisy or difficult

breathing when asleep and may wake up unrefreshed (because of their interrupted sleep), with a headache and a dry mouth. Disturbed sleep can result in the person being fatigued, sleepy, or irritable. Children particularly may experience behavioural difficulties and hyperactivity. In the long term, OSA places people at increased risk of cardiovascular conditions (such as high blood pressure, arrhythmia, heart attack, and stroke).

Up to 4 out of 5 children with PWS have OSA. People with PWS are at higher risk of OSA because of their floppy muscles (making it harder for the throat muscles to keep the airway open during sleep), small upper throat and jaw (narrowing the airway), thick mucus in the throat, weak breathing muscles, tendency to become overweight (placing more pressure on the airway and lungs), and tendency to scoliosis (reducing the amount of air that the lungs can hold).

There are several treatments for OSA including positioning during sleep, adenotonsillectomy (surgery to remove the tonsils and adenoids), and positive airway pressure (PAP) (which supports breathing by delivering air under pressure during sleep through a mask). Treatment of PWS with growth hormone can result in the development of OSA, and so children on growth hormone treatment need regular assessment with sleep studies to detect this.

Central sleep apnoea

People with PWS are also at risk of another type of problem with breathing during sleep called central sleep apnoea (CSA). This occurs where there are repetitive pauses in breathing or periods of very shallow breathing, resulting in low oxygen levels or a build-up of carbon dioxide in

the blood. The reason this condition occurs in PWS is not yet understood, but it may be related to the functioning of the brain to control breathing or it could be related to muscle weakness or scoliosis. People with PWS have a breathing control system that is less responsive to low oxygen and high carbon dioxide, and there is less likelihood that they will wake up or that their body will respond adequately to these signals. CSA and OSA can occur together and may make each other worse.

If central sleep apnoea is severe, it may require treatment with oxygen used during sleep at home, or with breathing support provided by a ventilator specially designed for home use.

Obstructive and central sleep apnoea are diagnosed by polysomnography, which is an overnight study of sleep and breathing, usually performed in a hospital sleep laboratory. For this test, many sensors are attached to the person's skin to measure their breathing, oxygen and carbon dioxide levels, and sleep quality.

Excessive daytime sleepiness

Many people with PWS get very drowsy during the daytime. This can be due to insufficient sleep or obstructive or central sleep apnoea, but can also be due to the reduced function of the hypothalamus. When excessive sleepiness is caused by problems with the hypothalamus, it is called narcolepsy. Up to 1 in 3 children and adults with PWS will develop narcolepsy. It is believed that this may be caused by the hypothalamus not secreting enough orexin (also called hypocretin), a hormone that regulates wakefulness (keeps the brain alert). People with PWS have low levels of this chemical in their cerebrospinal fluid (the fluid around

the brain and spinal cord). The lower the levels of orexin, the greater the daytime sleepiness. If a child with PWS is very sleepy during the day, it is important to discuss this with their paediatrician or respiratory physician.

There are several lines of treatment for excessive daytime sleepiness:

1. **Sleep routines** (e.g., bedtime; scheduled daytime naps) and **sleep environment** (e.g., temperature, darkness, removing distractions) can be modified.

2. **Treating night-time sleep problems** (e.g., OSA, CSA) to improve the quality of sleep at night will often reduce daytime sleepiness.

3. **Stimulant medications** can be used during the daytime to help keep the person awake.

Aspiration

Aspiration happens when food, drink, saliva, or some other substance goes down the wrong way, into the wind-pipe (trachea) instead of the food-pipe (oesophagus). Some children with PWS have weak swallowing muscles, especially when they are babies. This puts them at risk of aspiration.

Aspiration in PWS often isn't obvious. Children with PWS may aspirate without coughing or choking. They might have more subtle signs such as gurgly-sounding breathing or voice, red or watery eyes, or colour changes during or after mealtimes. Or these children may aspirate silently without any symptoms.

If there is any suspicion of aspiration, it is important to have it assessed because long-term aspiration can cause lung damage if untreated. Assessments can be done by a speech pathologist with expertise in dysphagia (difficulty swallowing) and by videofluoroscopy (a moving X-ray of the child while swallowing).

Weak chest muscles and respiratory illnesses

Babies with PWS, particularly if premature, may need respiratory support because their weak, floppy muscles make it difficult for them to get enough air into their lungs.

As these babies grow into childhood, their muscles become less weak and floppy. But their breathing muscles are still weaker than other children's. Compared with other children, children with PWS can hold less air in their lungs when they take a deep breath, and they cannot breathe in and out as fast or as hard as other children when they want to. This means that children with PWS have more difficulty clearing the phlegm (chest mucus) from their chests and are more liable to get chest infections.

Respiratory infections in PWS should also be treated very seriously because even an apparently mild chest infection can be life-threatening in children with PWS.

Children with PWS may not get a fever when unwell or may have a high pain threshold, and this makes diagnosis of illnesses difficult.

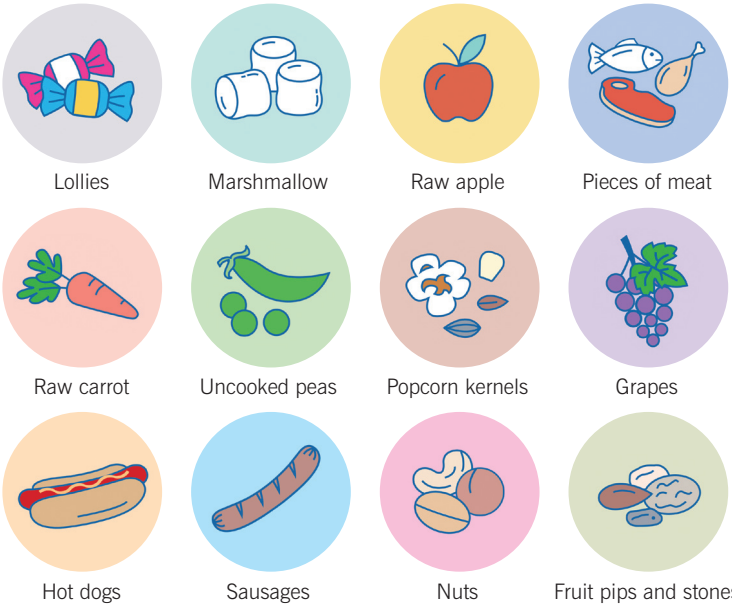
Choking

Children and adults with PWS are at risk of choking on food because their swallowing muscles are weak, their gag reflex sometimes doesn't work

properly, and they tend to swallow without chewing the food adequately. Choking is most common under the age of 5 years, but in PWS can occur at any age, even into adulthood. It is therefore recommended that:

- all meals be supervised by an adult,
- children with PWS avoid foods that cause choking (as shown in *Diagram 4*),
- parents know how to administer first aid if there is a choking incident.

Diagram 4: Foods that may cause choking



Behaviours and Emotions

Children with PWS are generally sociable, friendly, and loving. Many (not all) also have behaviour problems, such as meltdowns, insatiable appetite, anxiety, repetitive actions or thoughts, rigid adherence to routines, and challenges understanding social cues. There are many strategies and support websites to help manage these problems (links below on page 31). Clinical psychologists are specialists that can help families manage these problems.

Types of behavioural and emotional challenges

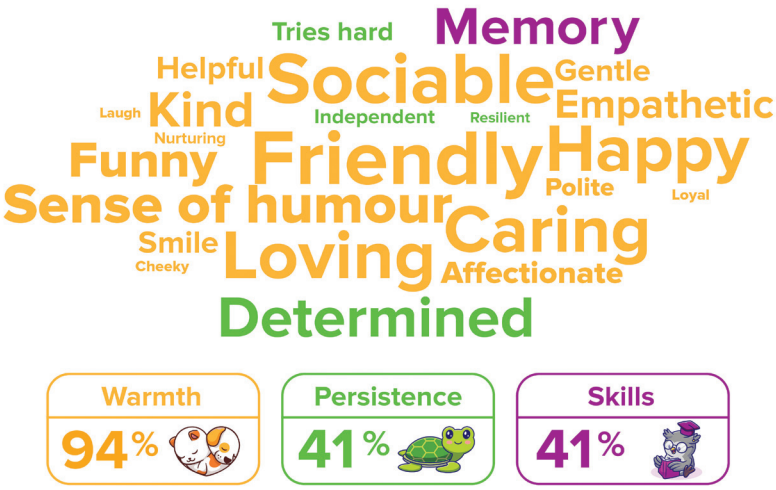
Many children and adults with PWS have behavioural and emotional challenges. These challenges seem to be caused by the genetic problems described earlier in this booklet. Some are food-related and some are not food-related. This section will describe the main challenges and how they are managed.

It is important to note that some of these behavioural and emotional challenges may resemble other conditions, but they have different causes and may need to be managed differently. For example, the food-related behaviours in PWS might seem similar to bulimia or obsessive compulsive disorder. But in PWS, they start at a much younger age, and they occur because the hypothalamus is unable to tell when these children have eaten enough—which is not the cause of bulimia or obsessive compulsive disorder. Similarly, some of the repetitive behaviours in PWS might look similar to Autism Spectrum Disorder (ASD). But children with ASD have a lot of other behaviours that children with PWS don't have.

Every child with PWS is different, so some children with PWS will show some of the behaviours described below and others will not. Some will have mild challenges, and others will have severe challenges.

It's also important to remember that children with PWS have a lot of behavioural and emotional strengths. In one study, 52 Australian parents of 4 to 24 year-olds with PWS talked about their personality strengths. Nearly all parents highlighted their children's warmth of personality, including friendliness, happiness, and empathy. In *Diagram 5*, the size of word corresponds to the number of parents who mentioned it.

Diagram 5: Characteristics of children with PWS in the words of their parents



Adapted from Figure 1 in Downs et al. Strengths and challenging behaviors in children and adolescents with Prader-Willi syndrome: Two sides to the coin. Am J Med Genet A 2022;188:1488-1496, with the following modifications:
(1) Australian spelling in place of American spelling; (2) themes indicated by colour instead of black-and-white patterning; (3) addition of icons to illustrate the themes.

Alongside these strengths, children with PWS may also have some of the behavioural and emotional challenges as described below.

Hyperphagia: Children with PWS may develop intense, persistent, insatiable hunger. This may start during early to mid childhood, often before 8 years of age. Children with PWS may become intensely focussed on food, persistently seek it out, steal food from other people, eat unhygienic foods (e.g., from bins) or non-foods (e.g., sand, grass, soap), and get up at night to get food. If they cannot get food, they may become distressed, which can lead to a meltdown.

Hyperphagia is currently managed by "food security", which means providing a clear meal schedule and restricting access to foods at other times, 24 hours a day in all settings (home, school, extended family and friends, community settings). With food security, food is kept out of sight, with locks on fridges and kitchen cupboards. Children with PWS are supervised for their safety to make sure they are not eating anything they shouldn't eat. Daily food schedules are used to plan what foods the child will eat and when meals and snacks will be served. Food security strategies have been shown to control children's food intake and reduce their food-related anxiety. An experienced dietitian or clinician can help to manage diet and behaviour.

Meltdowns: About 4 in 5 children with PWS have meltdowns or emotional outbursts. Their anger seems out of proportion to the trigger. A tantrum may start with repetitive questioning, and progress to crying, shouting, and, for some children, to kicking, hitting, lying on the ground, and throwing or damaging objects. However, not all children with PWS display aggressive behaviours in a meltdown. A meltdown can last for minutes or hours, typically longer for adolescents and adults than children. Occasionally, meltdowns can be averted by distracting the child when the first signs of agitation start to appear. However, often the child cannot control their emotions even if they want to, although they may be remorseful afterwards. One person with PWS said, "it is like sitting in a bubble outside of my body watching this monster come out of me that I don't know how to deal with!"

The reasons for meltdowns in PWS are not well understood. Individuals with PWS have meltdowns similar to a typical 2 to 3-year-old, but at a much older age. Their emotional regulation and coping skills in later childhood, adolescence and adulthood are thought to be similar to those of a young child.

Anxiety: Some children with PWS may become anxious, often in regard to food. This is shown by repetitive questioning to check that things are okay, loud or fast speech, trembling, agitated hand and body movements, and (in more verbal children) talk about worries and stress.

Perseveration: Some children with PWS may show the same behaviours repeated again and again, such as repetitive questioning, collecting items (e.g., rubber gloves), and following the same routine. Though these behaviours can be frustrating to families, people with PWS appear to find these rituals soothing (which is different from obsessive compulsive disorder).

Rigidity: From an early age, many children with PWS struggle with changes in familiar routines (e.g., changes in the way things are done, timing, order of events, places, travel routes). For example, if medication is given in a different way to usual, a child with PWS may find the change upsetting and not want to take the medication. If a parent drives to school via a different route from usual, a child with PWS might become distressed. Children with PWS also find it hard to switch between different tasks. They may hold strong opinions and have difficulty accepting other people's differing opinions, and this can lead to disagreements. This way of thinking isn't related to level of cognition: in PWS, children with normal intelligence are just as likely to struggle with changes in their environment or in their thinking as children with intellectual disability.

Social cognition: Children with PWS are usually friendly and social. But some find it hard to understand social cues and recognize other people's feelings, especially negative feelings (e.g., sadness, anger, fear). Neutral facial expressions can be misinterpreted as negative expressions, which can cause confusion and distress. This may make it hard for them to interact with their peers, and they may prefer to play with younger children than with children of their own age. They may stand too close to others without being aware of personal space. Older children and adults with PWS tend to have a strong sense of injustice and be quick to feel slighted by others, but not know how to adapt their own

behaviour to meet others' expectations. Children with PWS may show some behaviours that are similar to children with Autism Spectrum Disorder (ASD), but most often without meeting the full criteria for a diagnosis of ASD.

Important note: These behaviours make children with PWS vulnerable to exploitation and abuse from others. For example, they may be bribed by food to do things that they shouldn't. Because they don't always understand social norms, it means that they may not recognize inappropriate or risky behaviours. It is important to teach protective behaviours and to lay down simple, clear rules to guard against these situations (e.g., "Watch out: If anyone says to you 'Don't tell mummy' or 'let's have a secret,' it means that they want to do something bad. You need to tell mummy if that happens."). The child may be unable to talk about what is happening, so it is also important to be on the lookout for any changes in the child's behaviours that might indicate problems, and explore the reasons for these.

How to manage behavioural and emotional challenges

There are many strategies that can be used to manage behavioural and emotional challenges in PWS—more than can be covered in this booklet. *Table 2* gives a short summary of some of these strategies. For more information, please see the excellent resources listed below. Help for more severe problems is also available from healthcare professionals, especially clinical psychologists.

Table 2: Strategies for managing behavioural and emotional challenges in PWS. Summary of behavioural and emotional challenges.

Area	Strategies
Managing the environment to help people with PWS thrive	Food security; structured timetable and predicable routines; visual schedules; telling them beforehand what to expect (no surprises); positive language; calm voice; keep commands simple; use pictures to help communicate; reminders; humour; praise; reward system; set boundaries; set limit on number of questions they can ask; avoid bargaining/negotiating; consistent messages and responses from everyone; watch for early warning signs of tantrum and try to avert by distraction; help them with their transitions from one task to the next; watch for signs of changes in behaviour and plan accordingly or seek external help if needed.
Supporting a person with PWS through a meltdown	Safety first for child, others, and self (e.g., remove dangerous objects); give the child time and space to work through it and calm down; remove others from the child; talk calmly and say little; ignore or leave them alone if it's safe to do that; don't reason with them or get into arguments; try distraction and humour; don't give in to unreasonable demands; be careful not to let them learn that a tantrum leads to reward.
Strategies for the person with PWS	Relaxation techniques; thought blockers; hand-held computer game, puzzle, small toy, or stress ball to calm and distract; physical activity; practise coping strategies that can be used when crises arise (e.g., breathing exercises, counting, music); teach child to use band aids to cover sores and wounds (preventing skin-picking).

Resources for managing behavioural and emotional challenges:

PWSA UK – Support for those living with PWS: Behaviour management (*https://www.pwsa.co.uk/behaviour-management*), particularly this PDF on Behaviour management *(https://irp.cdn-website.com/1b38aac2/files/uploaded/06%20Behaviour%20management%20%28children%29%20generic.pdf)*

Behaviour and mental health in PWS (IPWSO and PWSA Ireland: *https://ipwso.org/information-for-families/behaviour-and-mental-health/*) (*https://www.youtube.com/watch?v=5MfuGXRXSKY*) – A video of parents of children and adults with PWS talking about how they manage their children's behaviour problems, followed by a presentation by Professor Tony Holland.

Behaviour page of PWS NZ (*https://www.pws.org.nz/support-management/behaviour*) – A range of PDF and video resources about managing behaviour in PWS.

Behaviour management page of PWS USA (*https://www.pwsausa.org/resources-a-z-behavior/*) – Fact sheets on different behaviour issues in PWS.

Mental health problems

Some people with PWS develop conditions that need psychiatric attention, mainly in adolescence and adulthood. These may include anxiety disorders, depression, oppositional defiant disorder, obsessive compulsive disorder, bipolar disorder, and psychotic disorders. If family members notice changes to the usual behaviour of a person with PWS, it is advisable to consult a psychiatrist. Professional help is available for people diagnosed with these conditions.

Sexual Development

In PWS, the genital organs are small and sexual development during puberty is slow. Men with PWS are infertile. Women with PWS have low fertility. Some children with PWS may benefit from sex steroids to induce puberty and improve bone health.

In both boys and girls with PWS, sexual organs are small, lower levels of sex hormones are secreted, and development during puberty is slow and often incomplete. These differences are more pronounced in boys than in girls.

In boys generally, the testes normally move down into the scrotum (descend) by 3 months of age. But in nearly all boys with PWS, one or both testes do not move down into the scrotum. This is called “undescended testes” and can be corrected by surgery (orchidopexy) or sometimes by non-surgical means.

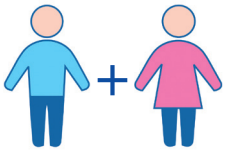
When they are born, boys with PWS may have a micropenis or “small penis”. In some boys it remains small.

Puberty in boys with PWS can occur within the expected age range, or early or late in some children. Puberty hormone replacement can be needed in adolescence or in later life. Men with PWS are infertile. Regular pubertal assessment is important throughout teenage years.

Up to 3 out of 4 girls with PWS are born with small external genital organs (labia minora and clitoris).

Puberty in girls with PWS starts at the expected time, but may progress more slowly than in girls without PWS. Girls may require hormone replacement if puberty does not progress normally.

Fertility is lower in women with PWS than in women without PWS. However, a few women with PWS have become pregnant and given birth.



About a third of boys and girls with PWS develop early signs that look like puberty (adrenarche), such as pimples, pubic and armpit hair, and body odour changes. This is not true puberty.

Treatment with sex steroids may be required in some children to induce puberty and development of secondary sexual characteristics. These pubertal hormones are also important for bone health.

Thinking and Learning

Children with PWS sometimes have learning difficulties in certain areas, such as reading, spelling, and maths. They may also be gifted in certain areas, such as solving puzzles. They may have difficulty reading other people's emotions.

Different children with PWS have very different levels of intelligence: some are at a normal level for their age, whereas others have more learning difficulties than most other children of the same age. Children with PWS tend to fall behind their classmates in subjects such as reading, spelling, and maths. At the same time, children with PWS may do much better than the classmates on jigsaw puzzles and word searches.

Children with PWS may understand things in a more concrete, literal way than most children would. So it can be hard for them to understand idioms, metaphors, and some jokes (even though they often have a very appealing sense of humour).

Children with PWS may have difficulty recognizing other people's emotions from their faces. They also have difficulty working out what another person thinks or believes based on their actions (e.g., realizing that a person carrying an umbrella must think it might rain). They find it difficult to see things from another person's point of view. They are less conscious of social norms (socially acceptable behaviours) than other children of the same age. So actions may seem shocking to them that

are not shocking to others (e.g., feeding pigeons in a park), whereas inappropriate actions (e.g., picking up an unknown baby from a pram) may seem okay.

For information about **schooling** for children with PWS, see:
https://ipwso.org/information-for-families/education-and-transition/

Activity

Children with PWS tend to be less active than other children. Physical activity is good for all children, and children with PWS enjoy joining physical activity programs. Children and adults with PWS enjoy many community activities, but these require special planning. Here are some hints and ideas.

Children and adults with PWS generally do less physical activity and spend more sedentary (sitting and lying) time than children and adults without PWS. Children and adults with PWS who do more physical activity have a higher muscle mass and stronger bones (higher bone mineral density). The World Health Organization's guidelines about physical activity are shown in *Table 3*.

Physical activity programs for children and adults with PWS are safe and effective for improving muscle mass and strength, walking distance, coordination, and bone mineral density. However, physical activity programs do not reduce body fat by themselves, unless they are extremely intensive and accompanied by dietary management. Children with PWS can join physical activity programs, their attendance rates are usually high (about 90%) and they rate such programs as moderately to highly enjoyable.

Activities outside the home are important for the quality of life of any child. Activities could include going to the shops, joining sporting clubs, walks in the community, or other special events. They can be valuable for

learning new skills, improving fitness, building social skills, and making friends. But when a child has PWS, they require special planning.

1. List the options. Assess your individual situation. Talk with family members, therapists, and support workers, and the person with PWS. Consider your child's skills and interests, how a new activity would fit into your family's usual schedules and activities, and who could support your child in their new activity.

Table 3: World Health Organization guidelines on physical activity in children and adults.

Age group	World Health Organization recommended physical activity levels
Children and adolescents (5-17 years)	• At least 60 minutes/day moderate to vigorous-intensity physical activity • Vigorous-intensity activities and bone-strengthening and muscle-strengthening activities at least 3 days/week • Limit sedentary activity
Adults aged 18-64 years	• At least 150–300 minutes/week moderate-intensity activity OR 75-150 minutes/week vigorous-intensity activity • Muscle-strengthening activities at least 2 days/week • Limit sedentary time; replace sedentary time with light activity
Adults aged over 65 years	• At least 150–300 minutes/week moderate-intensity activity OR 75-150 minutes/week vigorous-intensity activity • Muscle-strengthening activities at least 3 days/week • Varied multicomponent activities that emphasize balance and strength • Limit sedentary time; replace sedentary time with light activity

2. Consider what you're hoping to achieve with the new activity. Different activities will confer different benefits. So the choice of activity will depend on whether you're aiming for fitness, social skills, enjoyment, learning a new skill, independence, or something else.

3. Make sure you have the support you need to maintain this new activity. Inform the people involved about anything they need to know to help your child (e.g., dietary plans, how to manage behavioural issues, tips for motivating them). Supportive people and good rapport are critical for people with PWS: "With them I feel good because they treat me like a normal person, and they praise me every time I work with them."

Having PWS doesn't stop people from living rich and fulfilling lives out in the community. A child with PWS says, "I try to help people in trouble. I do a lot of activities such as swimming pool, occupational therapy, and kinesiotherapy because I have had back surgery twice for severe scoliosis." An adult with PWS says, "I do athletics, especially playing football and swimming. I go for walks with others, alone or with my dog. I like going to see my favourite football team play at the stadium. I play video-games and watch movies. I like going to see my favourite animal, the dolphin, at the dolphinarium."

Dental Hygiene

People with PWS tend to produce less saliva and may lack some permanent teeth, but they do not necessarily have more tooth decay than people without PWS. Like all children, it is recommended that children with PWS be taught from a young age to brush their teeth twice a day and have a dental check-up every 6 months.

Vision

Some eye conditions are more common in children with PWS than in other children. These include myopia (short-sightedness), which occurs in 41% people with PWS, and strabismus (squint), which occurs in 40% people with PWS. These conditions can be corrected, but they need careful monitoring.

Other Endocrine Conditions

A minority of people with PWS develop certain endocrine conditions. About one in three develop hypothyroidism Children with PWS should be screened yearly for hypothyroidism. A small percentage of people with PWS develop adrenal insufficiency, where the body does not produce enough cortisol. They are at risk of adrenal crisis, when the body is under stress. If overweight, people with PWS may develop Type 2 diabetes mellitus, especially in adulthood. All these conditions are treatable.

Apart from insufficient growth hormone, some other endocrine conditions can sometimes develop in people with PWS.

Hypothyroidism

Up to one third of people with PWS develop hypothyroidism.

Central hypothyroidism occurs when the pituitary gland does not direct the thyroid gland to secrete thyroid hormones as it should. It does not release enough Thyroid Stimulating Hormone (TSH).

Some people with PWS have **primary hypothyroidism**. Their bodies produce enough TSH; instead, their hypothyroidism is caused by problems with the thyroid gland itself.

Newborns with PWS normally do not have hypothyroidism, but they may develop this condition. Therefore, children with PWS should be screened

for hypothyroidism with a blood test by 3 months of age, and then yearly. Thyroid hormone levels may change after GH therapy begins because GH stimulates the body to produce thyroid hormone more rapidly.

Symptoms of hypothyroidism can be quite subtle, particularly central hypothyroidism. Symptoms include fatigue, sluggishness or sleepiness, feeling cold, dry skin, cradle cap (skin disease of the scalp in infants), constipation, difficulty concentrating, depression, and weight gain. Many of these symptoms are not unusual in PWS even without hypothyroidism, so these symptoms are in danger of being overlooked. If untreated, hypothyroidism has adverse effects on the heart and cardiovascular system. So, regardless of symptoms, yearly screening is recommended to ensure timely diagnosis and treatment.

Hypothyroidism is treated with levothyroxine, a thyroid replacement medication.

Adrenal insufficiency and adrenal crisis

A very small percentage of people with PWS secrete low levels of adrenocorticotropic hormone (ACTH) from their pituitary **(central adrenal insufficiency)**. ACTH is the hormone that tells the adrenal glands to produce cortisol. Consequently, people with low ACTH levels have insufficient cortisol **(hypocortisolism)** in response to stress.

Symptoms of adrenal insufficiency vary from person to person but may include fatigue, drowsiness, low blood pressure when standing or sitting up, poor colour with mottling of the skin, low blood glucose and muscle or joint pains. It can be treated by medication (glucocorticoids) which need to be taken daily for life.

People with adrenal insufficiency may go into **adrenal crisis**. This is a life-threatening condition that requires an immediate emergency treatment. Adrenal crisis can occur when the body has been under stress (e.g., illness, surgery). Therefore, affected individuals should have emergency plans in place to avoid adrenal crises and parents or caregivers need to learn how to administer intra-muscular hydrocortisone. People who are prone to adrenal crisis should wear a Medicalert bracelet.

Diabetes

The body has a multitude of chemical processes needed to process the nutrients in food, convert food to energy, and do its daily housekeeping chores (such as repairing cells, transporting oxygen to the cells, etc.). **Metabolism** is the name for all these chemical processes.

Children and adolescents with PWS sometimes have abnormalities of metabolism, including insulin resistance, associated with obesity. Type 2 diabetes mellitus can occur in up to one in four adults with PWS. This is associated with being severely overweight and at an older age during adulthood. Children who are overweight with PWS should have regular screening for the presence of diabetes to allow for early treatment.

Family Wellbeing

Having a child with PWS places extra demands on the whole family, including siblings. It can also give the families extra strengths. This section gives advice from other families with PWS about decision-making, planning, maintaining family wellbeing, and connecting with other families.

Pluses and minuses

Caring for a child with PWS places many extra demands on parents and siblings. Parents and siblings need to be vigilant at all times to protect the child with PWS from eating things they shouldn't eat and to deal with any emotional outbursts. There is more unpredictability. Parents need to give more time to the child with PWS, and there is less time for one another and for their other children. Consequently, families of children with PWS may have higher levels of stress than other families. At the same time, some families also say that this experience gives them extra strengths. For example, some siblings say that from their sibling with PWS they learnt to be resilient, kind, patient, to accept people who are very different from themselves, to help others, to be more independent, and to love somebody unconditionally.

Planning and decision-making

The child with PWS is part of a family unit, and the decisions affect everyone, so it's good to be transparent. One dad of a child with PWS said, "Hold brief family meetings with everyone. We get even the little ones in on it. Then we can talk things out calmly, set ground rules,

especially for food." An adult with PWS said, "My parents are the closest and most valuable people. They are strict but affectionate and loving. I am always looking for contact with them, even if I have made them angry. My brothers are also close to me. One of them is playful, and the other one is protective, a little severe. With them, I am calm and feel protected."

Caring for a child with PWS requires more planning and organizing. One adult needs to supervise the child all the time. It's important to plan times for a parent to be alone with the other child or children in the family too, and do something nice together or just enjoy one another's company. Parents need to watch out for signs of anxiety, depression, or distress in the siblings of a child with PWS. Parents also need to find time to support one another and maintain that essential bond. A mother of a child with PWS said, "If nothing else, we spend time talking on the phone together… about things important to us or one of us… you'd be surprised it works… you feel better and connected even though I'm home and he's out".

Whole of family wellbeing

Parents of children with PWS say it's important to give priority to maintaining the whole family's health and wellbeing. That includes the routine things (like keeping up to date with dental checks-ups and immunizations) and the activities that contribute to everyone's quality of life (like going for walks together, doing jobs around the house together, maintaining hobbies, and having stress-release strategies such as meditation and yoga). Parents also find it useful to connect with local groups (though these need to be chosen carefully), such as pet therapy, horse riding, churches, and community organizations where food intake can be supervised.

Siblings of a child with PWS

It's good to give the other children in the family information about PWS when they are ready to receive it. The more they learn, the better they will be able to understand and respond to their sibling with PWS. It's also important to give them a chance to discuss their concerns with you in the absence of their sibling with PWS. One concern that will need to be discussed is the role of the siblings when the parents are no longer able to care for or be legally responsible for the person with PWS. The earlier this is discussed, the better, because then preparations can be made well ahead of time.

Support and resources

Other families with children with PWS and PWS organizations also provide lots of support and resources. There are national and state based Facebook support groups. The support becomes reciprocal: "Help the newcomers, the ones with babies just diagnosed. They're frightened. I always try to help new ones feel better. Then I feel better too."

For more information on family life, see this website: *https://www.pwsa.co.uk/family-life*.

For more information on siblings, see this website: *https://www.pws.org.nz/support-management/for-siblings*.

For more information on health and wellness for a family with PWS, see this website: *https://www.pwsausa.org/healthandwellness/*.

Giving Information to People Who Don't Know your Child

PWS is a very rare disorder, and so many people in the community will know nothing about it. Some families of a child with PWS like to have a one-page summary of information about their child that they can quickly give to strangers who need to take responsibility for their child, especially if emergency situations arise (e.g., ambulance workers, police). Having an information page ready to hand to strangers will help them to work safely with your child, to understand his/her behaviours (e.g., in regard to food, anxiety about changes in routine), and to know how to manage situations as they arise.

About My Child

My child, _____, was born Prader-Willi syndrome (PWS), a rare genetic condition. PWS can affect a lot of different body functions. I have ticked the ones that apply to us. I've written extra notes where needed.

- ☐ An interest in food, insatiable appetite. Needs close supervision to prevent excessive eating.
- ☐ Sleep disturbances or sleep apnoea.
- ☐ Excessive daytime sleepiness.
- ☐ Weak floppy muscles (hypotonia).
- ☐ Chest and breathing problems and tendency to chest infections (can become very serious).
- ☐ Tendency for food to go down the wrong way or to choke on food.
- ☐ A friendly, caring personality, but can have sudden, uncontrollable meltdowns (e.g when regular routine is interrupted).
- ☐ Tendency to become anxious and need repeated reassurances.
- ☐ Difficulties with thinking and learning (e.g., understanding conventions of social interactions).

My child's current medications (including medicines, tablets, injections) are as follows:

Where To Go For Help and Support

Prader-Willi Syndrome Australia (*pws.org.au*) supports better outcomes by bringing together people, resources and up to date information.

Siblings Australia (*siblingsaustralia.org.au*) is committed to improving the support available for siblings of children and adults with chronic conditions including disability, chronic illness and mental health issues.

International Prader-Willi Syndrome Organization (*ipwso.org*) has a lot of useful information for families of children with PWS on their website.

The National Disability Insurance Scheme (NDIS) (*ndis.gov.au*) funds children and adults with a disability in Australia. You need to apply to NDIS for funding. When your child's funding has been approved, you can plan your priorities for your child and plan how your funding will be used. This website shows you how to apply for funding and plan how you will use it.

Glossary

Adrenal glands
Endocrine glands situated above the kidneys. They release several hormones, including adrenaline, sex steroids, and cortisol. They regulate important body functions, including blood pressure and the body's response to stress.

Adrenocorticotropic hormone (ACTH)
A hormone released by the anterior pituitary lobe. It controls the body's cortisol production.

Aspiration
Inhaling food, drink, saliva, or some other substance. It can lead to coughing, gurgling or choking or it can be silent.

Autism Spectrum Disorder (ASD)
A developmental disability that can make it hard to communicate socially and interact socially. Children with ASD may also have restricted and repetitive patterns of activities and interests.

Bariatric surgery
Surgery that reduces the size of the stomach to make a person feel as though they have eaten enough after a smaller meal.

Blood glucose
Level of sugar in the blood. Blood glucose needs to be kept within certain limits (not too high or too low). Diabetes occurs when blood glucose levels become too high.

Bulimia
An eating disorder. Binge eating is followed by severe methods to control weight gain (such as self-induced vomiting, laxatives, excessive exercise).

Central adrenal insufficiency
A condition in which the body does not produce enough cortisol.

Central sleep apnoea
A condition in which there are repetitive pauses in breathing during sleep or periods of very shallow breathing.

Cortisol
A hormone produced by the adrenal glands. It regulates the body's response to stress, affects blood sugar levels, and affects other systems including blood pressure and the immune system.

Endocrine system
A network of organs that release hormones into the bloodstream to regulate many body functions. Endocrine organs include the hypothalamus, pituitary gland, thyroid, parathyroid, adrenal glands, pancreas, ovaries, and testes.

FISH (fluorescence in-situ hybridization) test
A blood test that can detect whether a person has PWS by paternal 15q11-q13 deletion.

Ghrelin
A hormone that stimulates hunger.

Growth hormone
A hormone that stimulates growth of the body . Also called somatotropin.

Hormones
Chemical messengers released by endocrine organs into the bloodstream.

Hyperphagia
Intense, persistent, insatiable hunger. Even after eating enough, the person still feels the need to eat more.

Hypocortisolism
Primary adrenal insufficiency, a condition in which the adrenal glands do not produce enough hormones, particularly cortisol.

Hypothalamus
A structure in the brain that helps to control many body functions (including body temperature, hunger and thirst, growth, sexual functions, emotions and behaviour, sleep).

Hypothyroidism
A condition in which the thyroid gland does not produce enough thyroid hormone. This causes fatigue, weight gain and other symptoms.

Imprinting defect
Changes to genes, such as microdeletions (where a very small number genes are deleted) and epi-mutations (which affect the way the genes function).

Insulin
A hormone produced by the pancreas. It regulates blood sugar (glucose) levels. In diabetes, the body does not produce enough insulin and blood glucose becomes too high.

Maternal uniparental disomy (mUPD)
This occurs when person inherits two copies of chromosome 15 from their mother and none from their father. It is one cause of Prader-Willi syndrome.

Metabolism
The innumerable chemical processes that the body performs continually to maintain itself (e.g., converting the nutrients into energy, repairing cells, transporting oxygen to the cells).

Methylation test
A blood test that can detect whether a person has PWS.

Narcolepsy
A condition of excessive daytime sleepiness. It is caused by problems with the hypothalamus.

Obsessive Compulsive Disorder (OCD)
An anxiety disorder. A person with OCD repeatedly has unwanted thoughts (obsessions) and feel they need to perform certain repetitive actions (compulsions). These cause the person distress.

Obstructive sleep apnoea
A condition in which there is repetitive obstruction of the upper airway (nose and throat) during sleep.

Orchidopexy
A surgical procedure to move undescended testes down into the scrotum.

Orexin
A hormone that regulates wakefulness. Also known as hypocretin.

Ovaries
Endocrine glands either side of the uterus in females. They produce eggs and release hormones that regulate menstruation and pregnancy.

Pancreas
An organ situated behind the stomach. It belongs to the digestive system and the endocrine system. It regulates digestion and blood sugar levels. It releases several hormones, including insulin.

Parathyroid glands
Endocrine glands situated behind the thyroid gland. They regulate blood calcium levels.

Paternal 15q11-q13 deletion
This occurs when a person inherits a chromosome 15 from their father in which the 15q11-q13 region is missing. It is the most common cause of Prader-Willi syndrome.

Pituitary gland
An endocrine gland situated under the hypothalamus. It releases many hormones that affect body functions (e.g., growth, blood sugar levels, reproductive function).

Prader-Willi syndrome (PWS)
A rare neurodevelopmental condition caused by changes to certain genes on Chromosome 15. It can have effects on many body functions, including appetite, muscle tone, growth, sleep, emotions and behaviour, and breathing.

Rigidity
A person with mental rigidity has difficulty seeing things from another person's point of view and changing their own point of view.

Scoliosis
A condition in which the spine curves sideways.

Social cognition
Understanding of social and inter-personal situations and how to interact with other people.

Somatotropin
Another name for growth hormone.

Testes
Endocrine glands situated in the scrotum (bag behind the penis) in males. They produce sperm and release the male sex hormone, testosterone.

Thyroid gland
An endocrine gland in the throat that regulates some of the body's metabolic processes (e.g., heart rate, blood pressure, body temperature, body weight).

Thyroid Stimulating Hormone (TSH)
A hormone released by the anterior pituitary lobe. It stimulates the thyroid to produce hormones that affect how the body manages food and energy.

Translocation
Genetic changes in which a chromosome has broken and one part of it has attached to a different chromosome.

Type 2 diabetes mellitus
A condition in which blood sugar levels are too high.

Videofluoroscopy
A moving X-ray while swallowing.

References

Growth and growth hormone

Aycan Z, Baş VN. Prader-Willi syndrome and growth hormone deficiency. J Clin Res Pediatr Endocrinol 2014;6:62-67.

Driscoll DJ, Miller JL, Schwartz S, Cassidy SB. Prader-Willi Syndrome. In: Adam MP, Ardinger HH, Pagon RA, et al., eds. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle., 1998 [Updated 2017 Dec 14].

Deal CL, Tony M, Hoybye C, et al. Growth Hormone Research Society workshop summary: consensus guidelines for recombinant human growth hormone therapy in Prader-Willi syndrome.
J Clin Endocrinol Metab 2013;98:E1072-1087.

Tauber M, Hoybye C. Endocrine disorders in Prader-Willi syndrome: a model to understand and treat hypothalamic dysfunction. Lancet Diabetes Endocrinol 2021;9:235-246.

Vogt KS, Emerick JE. Growth Hormone Therapy in Adults with Prader-Willi Syndrome. Diseases 2015;3:56-67.

Pacoricona Alfaro DL, Lemoine P, Ehlinger V, et al. Causes of death in Prader-Willi syndrome: lessons from 11 years' experience of a national reference center. Orphanet J Rare Dis 2019;14:238.

van Bosse HJP, Butler MG. Clinical Observations and Treatment Approaches for Scoliosis in Prader-Willi Syndrome. Genes (Basel) 2020;11.

Body weight and eating

Theodoro MF, Talebizadeh Z, Butler MG. Body composition and fatness patterns in Prader-Willi syndrome: comparison with simple obesity. Obesity (Silver Spring) 2006;14:1685-1690.

Muscogiuri G, Barrea L, Faggiano F, et al. Obesity in Prader-Willi syndrome: physiopathological mechanisms, nutritional and pharmacological approaches. J Endocrinol Invest 2021;44:2057-2070.

Ragusa L, Crinò A, Grugni G, et al. Caring and living with Prader-Willi syndrome in Italy: integrating children, adults and parents' experiences through a multicentre narrative medicine research. BMJ Open 2020;10:e036502.

Tan Q, Orsso CE, Deehan EC, et al. Current and emerging therapies for managing hyperphagia and obesity in Prader-Willi syndrome: A narrative review. Obes Rev 2020;21:e12992.

Vitale SA. Parent Recommendations for Family Functioning With Prader-Willi Syndrome: A Rare Genetic Cause of Childhood Obesity. J Pediatr Nurs 2016;31:47-54.

Morales JS, Valenzuela PL, Pareja-Galeano H, Rincón-Castanedo C, Rubin DA, Lucia A. Physical exercise and Prader-Willi syndrome: A systematic review. Clin Endocrinol (Oxf) 2019;90:649-661.

Liu SY, Wong SK, Lam CC, Ng EK. Bariatric surgery for Prader-Willi syndrome was ineffective in producing sustainable weight loss: Long term results for up to 10 years. Pediatr Obes 2020;15:e12575.

Breathing and sleep

Mackay J, McCallum Z, Ambler GR, et al. Requirements for improving health and well-being of children with Prader-Willi syndrome and their families. J Paediatr Child Health 2019;55: 1029-1037.

Nixon GM, Brouillette RT. Sleep and breathing in Prader-Willi syndrome. Pediatr Pulmonol 2002;34:209-217.

Arens R, Gozal D, Burrell BC, et al. Arousal and cardiorespiratory responses to hypoxia in Prader-Willi syndrome. Am J Respir Crit Care Med 1996;153:283-287.

Tan HL, Urquhart DS. Respiratory Complications in Children with Prader Willi Syndrome. Paediatr Respir Rev 2017;22:52-59.

Ghergan A, Coupaye M, Leu-Semenescu S, et al. Prevalence and Phenotype of Sleep Disorders in 60 Adults With Prader–Willi Syndrome. Sleep 2017;40.

Sedky K, Bennett DS, Pumariega A. Prader Willi syndrome and obstructive sleep apnea: co-occurrence in the pediatric population. J Clin Sleep Med 2014;10:403-409.

Cataldi M, Arnaldi D, Tucci V, et al. Sleep disorders in Prader-Willi syndrome, evidence from animal models and humans. Sleep Med Rev 2021;57:101432.

Stevenson DA, Heinemann J, Angulo M, et al. Deaths due to choking in Prader-Willi syndrome. Am J Med Genet A 2007;143a:484-487.

Behaviours and emotions

Holland AJ, Aman LCS, Whittington JE. Defining Mental and Behavioural Disorders in Genetically Determined Neurodevelopmental Syndromes with Particular Reference to Prader-Willi Syndrome. Genes (Basel) 2019;10.

Whittington J, Holland A. A review of psychiatric conceptions of mental and behavioural disorders in Prader-Willi syndrome. Neurosci Biobehav Rev 2018;95:396-405.

Downs J, Blackmore AM, Chen W, Nixon GM, Choong CS. Strengths and challenging behaviors in children and adolescents with Prader-Willi syndrome: Two sides to the coin. Am J Med Genet A 2022;188:1488-1496.

Schwartz L, Caixàs A, Dimitropoulos A, et al. Behavioral features in Prader-Willi syndrome (PWS): consensus paper from the International PWS Clinical Trial Consortium. J Neurodev Disord 2021;13:25.

Caitlin. Available at: https://www.fpwr.org/blog/its-not-normal-its-better-a-letter-to-prader-willi-siblings. Accessed 20/9/2022.

Rice LJ, Einfeld SL. Cognitive and behavioural aspects of Prader-Willi syndrome. Curr Opin Psychiatry 2015;28:102-106.

Shriki-Tal L, Avrahamy H, Pollak Y, et al. Psychiatric disorders in a cohort of individuals with Prader-Willi syndrome. Eur Psychiatry 2017;44:47-52.

Feighan SM, Hughes M, Maunder K, Roche E, Gallagher L. A profile of mental health and behaviour in Prader-Willi syndrome. J Intellect Disabil Res 2020;64:158-169.

Activity

Whittington J, Holland A. Cognition in people with Prader-Willi syndrome: Insights into genetic influences on cognitive and social development. Neurosci Biobehav Rev 2017;72:153-167.

Dykens EM. Are jigsaw puzzle skills 'spared' in persons with Prader-Willi syndrome? J Child Psychol Psychiatry 2002;43:343-352.

Lo ST, Siemensma E, Collin P, Hokken-Koelega A. Impaired theory of mind and symptoms of Autism Spectrum Disorder in children with Prader-Willi syndrome. Res Dev Disabil 2013;34:2764-2773.

Ragusa L, Crinò A, Grugni G, et al. Caring and living with Prader-Willi syndrome in Italy: integrating children, adults and parents' experiences through a multicentre narrative medicine research. BMJ Open 2020;10:e036502.

Bellicha A, Coupaye M, Mosbah H, Tauber M, Oppert JM, Poitou C. Physical Activity in Patients with Prader-Willi Syndrome-A Systematic Review of Observational and Interventional Studies. J Clin Med 2021;10.

Shields N, Westle A, Bennell KL, Taylor NF. Physiotherapists perceived developing positive rapport facilitates participation in exercise among people with Prader-Willi Syndrome: a qualitative study. Disabil Rehabil 2020;42:3475-3480.

Dental hygiene

Saeves R, Nordgarden H, Storhaug K, Sandvik L, Espelid I. Salivary flow rate and oral findings in Prader-Willi syndrome: a case-control study. Int J Paediatr Dent 2012;22:27-36.

Ritwik P, Vu J. Bridging Oral and Systemic Health in Children with Prader-Willi Syndrome: Case Reports and Dental Treatment Recommendations. Curr Pediatr Rev 2021;17:336-344.

Vision

Bohonowych JE, Vrana-Diaz CJ, Miller JL, McCandless SE, Strong TV. Incidence of strabismus, strabismus surgeries, and other vision conditions in Prader-Willi syndrome: data from the Global Prader-Willi Syndrome Registry. BMC Ophthalmol 2021;21:296.

Hypothyroidism

Pellikaan K, Snijders F, Rosenberg AGW, et al. Thyroid Function in Adults with Prader-Willi Syndrome; a Cohort Study and Literature Review. J Clin Med 2021;10.

Iughetti L, Vivi G, Balsamo A, et al. Thyroid function in patients with Prader-Willi syndrome: an Italian multicenter study of 339 patients. J Pediatr Endocrinol Metab 2019;32:159-165.

Adrenal insufficiency and adrenal crisis

Tauber M, Hoybye C. Endocrine disorders in Prader-Willi syndrome: a model to understand and treat hypothalamic dysfunction. Lancet Diabetes Endocrinol 2021;9:235-246.

Angulo MA, Butler MG, Cataletto ME. Prader-Willi syndrome: a review of clinical, genetic, and endocrine findings. J Endocrinol Invest 2015;38:1249-1263.

Kusz MJ, Gawlik AM. Adrenal insufficiency in patients with Prader-Willi syndrome. Front Endocrinol (Lausanne) 2022;13:1021704.

Family wellbeing

Rae-Seebach RD. The impact of Prader-Willi syndrome on healthy siblings' perceptions of caregiving availability and psychosocial adjustment. Palo Alto, CA2008.

Mazaheri MM, Rae-Seebach RD, Preston HE, et al. The impact of Prader-Willi syndrome on the family's quality of life and caregiving, and the unaffected siblings' psychosocial adjustment. J Intellect Disabil Res 2013;57:861-873.

Vitale SA. Parent Recommendations for Family Functioning With Prader-Willi Syndrome: A Rare Genetic Cause of Childhood Obesity. J Pediatr Nurs 2016;31:47-54.

Merck is proud to bring you this booklet from the *Hormones and Me* educational series. We aim to provide readers with a better understanding of the issues relating to endocrine disorders particularly in children. We hope that you find it a valuable and helpful resource.

Please ask your doctor or nurse for further information on the resources available to you.

The ***Hormones and Me*** series includes:

Congenital Adrenal Hyperplasia (CAH)

Congenital Hypothyroidism

Craniopharyngioma

Delayed Puberty

Diabetes Insipidus

Disorders of the Thyroid Gland in Children and Adolescents

Growth Problems in Children

Klinefelter Syndrome

Management of Emergency or 'Stress' Situations where Hypoglycaemia or Cortisol Deficiency Occur

Multiple Pituitary Hormone Deficiency (MPHD)

Prader Willi Syndrome

Puberty and its Problems

Turner Syndrome

DISCLAIMER

Speak to an appropriate healthcare professional

The information contained in this booklet is intended for educational purposes only and should not be relied upon, or otherwise used, in place of medical advice.

The information contained in this booklet is not provided in the course of a professional relationship between healthcare provider and patient and it is not intended to create any patient relationship. Any medical information contained in this booklet is not intended as a substitute for informed medical advice. You should consult with an appropriate healthcare professional on (1) any specific problem or matter which is covered by information in this booklet before taking any action; or (2) for further information or to discuss any questions or concerns. You should never disregard medical advice or delay seeking the advice of a healthcare professional based on something you have read in this booklet. You fully understand and acknowledge that the information contained in the booklet is not intended or designed to diagnose, prevent, treat or provide a cure for any condition or disease, to ascertain the state of your health, or to be substituted for professional medical care. We encourage you to seek the advice of your healthcare professional if you have any questions or concerns arising from the information contained in the booklet.

The content of this booklet has been created by the members of the Australian and New Zealand Society for Paediatric Endocrinology and Diabetes (ANZSPED), without transfer of any value from Merck Healthcare Pty. Ltd. Merck Healthcare Pty. Ltd.'s participation is limited to: (i) granting of the right to use the Hormones and Me booklet in favor of ANZSPED; and (ii) sponsoring the editing of this booklet conducted by a third party vendor.

Whilst the parties have taken reasonable steps to ensure the accuracy of the contents of this booklet, it is provided on an "AS IS" basis and on the terms and understanding that Merck Healthcare Pty Ltd. (and their respective officers and employees) and all other persons involved in the writing, development, publication, distribution, sponsorship or endorsement of this booklet, to the fullest extent permitted by applicable law, are not responsible for (1) any error or any omission from this booklet; (2) make no warranties, representations or give any undertakings either express or implied about any of the content of this booklet (including, without limitation the timeliness, currency, accuracy, correctness, completeness or fitness for any particular purpose of the booklet or its content); (3) are not responsible for the results of any action or inaction taken on the basis of any information in this booklet; (4) are not engaged in rendering any medical, professional or other advice or services; (5) expressly disclaim any and all liability and responsibility to any person in respect of anything done by any such person in reliance, whether wholly or partially, upon the whole or any part of the contents of this booklet.

To the fullest extent permitted by applicable law, IN NO EVENT SHALL MERCK HEALTHCARE PTY LTD. BE LIABLE FOR PERSONAL INJURY, OR ANY INCIDENTAL, SPECIAL, INDIRECT OR CONSEQUENTIAL DAMAGE WHATSOEVER AND HOWSOEVER ARISING, INCLUDING BUT NOT LIMITED TO, DAMAGES FOR LOSS OF PROFITS ARISING OUT OF OR RELATED TO THE USE OF THE BOOKLET UNDER ALL HEADS OF LIABILITY (WHETHER IN CONTRACT, TORT OR OTHERWISE).

Merck Healthcare Pty Ltd. will not be held responsible for the content , accuracy or completeness of the information presented and the references and external third party website links contained in the booklet.

Merck Healthcare Pty Ltd | ABN 72 006 900 830 Suite 1 | Level 1 | Building B |
11 Talavera Road | Macquarie Park NSW 2113 | Australia
Phone: 1800 257 348

Date of preparation: March 2024 | AU-NONE-00026

Hormones and Me

Prader-Willi Syndrome

This booklet is valuable reading for anyone with Prader-Willi Syndrome.

It is also recommended reading for their family and friends.