Prader – Willi Syndrome: An Assessment of Genetics, Ghrelin and Lifestyle

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Abstract

Prader-Willi syndrome is the first genetic syndrome found to cause obesity, as well as the most “commonly identified genetic cause of obesity”. Prader-Willi syndrome results from a lack of expression from the paternal gene on chromosome 15q11-q13 (1-5). Prader-Willi presents symptoms including severe neonatal hypotonia, hyperphagia, hypogonadism, learning disabilities and behavioral problems. Confirmation of Prader-Willi syndrome requires genetic testing. DNA methylation analysis is the only genetic test that can determine if an individual has Prader-Willi syndrome or not. Children with Prader-Willi syndrome often have behavioral problems such as temper tantrums, as well as sleep disturbances, skin picking and a high pain threshold. Almost all children with Prader-Willi syndrome display delayed motor development, such as not sitting up until twelve months and not walking until twenty-four months.

Growth hormone therapy is thought to improve growth rate, body composition, muscle function and energy level. Many times, if growth hormone treatment is begun early on in life, the physical characteristics of Prader-Willi syndrome are avoidable.

Ghrelin is an orexigenic gastric hormone that is secreted in the duodenum, pancreas, pituitary, hypothalamus, testis, ovary, bone and cartilage. Ghrelin stimulates hunger, which in turn often increases the intake of food causes fat utilization to decrease in humans. It has been found that individuals with Prader-Willi syndrome have elevated levels of plasma ghrelin after fasting. In healthy obese patients there is a negative correlation between body mass index and ghrelin, however this was not observed in children with Prader-Willi syndrome. The current review of literature focuses on Prader-Willi syndrome as a whole as well as the genetic components, effects of ghrelin on the body and lifestyle.
Introduction

Obesity is a significant health issue among children and adolescents in today’s society. However, obesity does not just affect normal children and adolescents, but disabled children as well. Children with disabilities are more likely to develop chronic conditions and other health conditions associated with their primary disabilities (Neter et al, 2011).

A study conducted in the Netherlands evaluated schools that offer special education to children who have a mental or physical disability, have multiple disabilities or have a chronic disease (Neter et al, 2011). The study found that the prevalence of overweight and obese children was significantly higher in disabled children than nondisabled children ($p < .001$) (Neter et al, 2011). Children with disabilities were found to be three (30.6%) times overweight than nondisabled children (9.9%) (Neter et al, 2011). Similarly children with disabilities (10.6%) were found to be six times more obese than nondisabled children (1.8%) (Neter et al, 2011).

Prader-Willi syndrome was first discovered in 1956 by Prader, Labhart and Willi, as the first human disease attributed to genomic imprinting (Mahgoub, 2007; Cassidy and Driscoll, 2009; Chen et al, 2010; Ho and Dimitropoulos, 2010). Prader-Willi syndrome is the first genetic syndrome found to cause obesity, as well as the largest known genetic cause of obesity (Wattendorf and Muenke 2005; Yearwood et al, 2011). Prader-Willi syndrome results from a lack of the paternal chromosome 15q11-q13 (1-5) being expressed (Goldstone et al, 2008). Prader-Willi presents symptoms including severe neonatal hypotonia, hyperphagia, hypogonadism, learning disabilities and behavioral problems (Goldstone et al, 2008). Individuals with Prader-Willi syndrome are on average short with small hands and feet, obese, have a narrow bifrontal diameter, full cheeks and almond shaped eyes (Ho and Dimitropoulos, 2010).

Prader-Willi syndrome is found in approximately 1/25,000 births (Wattendorf and
Muenke 2005; Ho and Dimitropoulos, 2010). This means that there is a .004% chance that a child will be born with Prader-Willi syndrome. Most parents who have a child with Prader-Willi syndrome will not face a great risk of having another child with Prader-Willi syndrome, however genetic testing can provide a more detailed risk for each family (Wattendorf and Muenke 2005). Prader-Willi syndrome affects both males and females equally, and is not found in any one single race (Wattendorf and Muenke 2005; Yearwood et al, 2011).

Confirmation of Prader-Willi syndrome requires genetic testing. DNA methylation analysis is the only genetic test that can determine if an individual has Prader-Willi syndrome or not (Goldstone et al, 2008; Yearwood et al, 2011; Cassidy and Driscoll, 2009). It is important to undergo genetic testing as Angelman Syndrome, Fragile X Syndrome, UPD 14, Cohen Syndrome, Bardet – Biedl Syndrome and Alström Syndrome all have similar characteristics to Prader-Willi syndrome (Cassidy and Driscoll, 2009). A fluorescence in situ hybridization (FISH) test can be performed by taking a sample from the proband to detect the presence of chromosome 15q11-q13 (Goldstone et al, 2008). If the presence of chromosome 15q11-q13 is negative, it does not discount a Prader-Willi syndrome diagnosis, and should be confirmed with DNA methylation (Goldstone et al, 2008). After a positive DNA methylation analysis, another test called a DNA polymorphism analysis, should be performed to help confirm a diagnosis of Prader-Willi syndrome (Goldstone et al, 2008). The DNA polymorphism analysis is performed on the proband and the parents to determine if the individual with Prader-Willi syndrome has the maternal uniparental disomy or an imprinting defect (Goldstone et al, 2008). The family who previously had a child diagnosed with Prader-Willi syndrome, who has an imprinting defect, has a 50% recurrence risk if the father is the carrier of the imprinting deletion (Goldstone et al, 2008). A prenatal diagnosis is very difficult to make and rarely occurs (Goldstone et al, 2008).
Clinical diagnosis of Prader-Willi syndrome is available, but must be confirmed with the aforementioned genetic testing. For an individual to be clinically diagnosed with Prader-Willi syndrome, he or she must present four major criteria and one minor criteria as shown in Figure 1 from Wattendorf and Muenke. (Cassidy and Schwartz, 2009).

![Figure 1. Diagnostic Criteria for Prader-Willi Syndrome](Wattendorf and Muenke, 2005)

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic facial features (may include almond-shaped eyes, down-turned mouth, narrow bifrontal diameter, strabismus, thin upper lip; see Figures 1 and 2)</td>
<td>Decreased fetal movement and infantile lethargy</td>
</tr>
<tr>
<td>Developmental delay</td>
<td>Esotropia, myopia</td>
</tr>
<tr>
<td>Feeding problems/failure to thrive during infancy</td>
<td>Hypogammination</td>
</tr>
<tr>
<td>Hypogamnism (may include cryptorchidism, hypoplastic scrotum, and small testes in males; hypoplastic labia minora and clitoris in females; and pubertal deficiency)</td>
<td>Narrow hands with straight ulnar border</td>
</tr>
<tr>
<td>Infantile central hypotonia</td>
<td>Short stature (compared with family members)</td>
</tr>
<tr>
<td>Rapid weight gain between 1 and 6 years of age</td>
<td>Skin picking</td>
</tr>
</tbody>
</table>

*Note: Score 1 point for each major criterion and 0.5 point for each minor criterion. A diagnosis of Prader-Willi syndrome should be suspected in children younger than three years with a score of at least 5; and in children three years and older with a score of at least 8, with 4 points from major criteria. Supportive criteria (no points) include high pain threshold, decreased vomiting, temperature control problems, scoliosis, kyphosis, early adrenarche, osteoporosis, unusual skill with jigsaw puzzles, and normal neuromuscular studies.*

Information from reference 4.

![Figure 2. Clinical Manifestations of Prader-Willi Syndrome](Yearwood et al, 2011)

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
<th>Supportive Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic facial features: narrow bifrontal diameter, almond-shaped palpebral fissures, down-turned mouth, strabismus, thin upper lip</td>
<td>Decreased fetal movement and infantile lethargy, improving with age</td>
<td>High pain threshold</td>
</tr>
<tr>
<td>Developmental delay/mild-to-moderate intellectual disabilities/multiple learning disabilities</td>
<td>Typical behavior problems, including temper tantrums, obsessive-compulsive behavior, stubbornness, rigidity, stealing, and lying</td>
<td>Decreased vomiting</td>
</tr>
<tr>
<td>Hyperphagia</td>
<td>Sleep disturbance/insomnia</td>
<td>Scoliosis and/or kyphosis</td>
</tr>
<tr>
<td>Hypogamnism manifest as genital hypoplasia; small labia minora and clitoris in females; hypoplastic scrotum and cryptorchidism in males; incomplete and delayed puberty; infertility</td>
<td>Narrow hands with straight ulnar border</td>
<td>Early adrenarche</td>
</tr>
<tr>
<td>Neonatal and infantile central hypotonia with poor suck, improving with age</td>
<td>Esotropia, myopia</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Feeding problems and/or failure to thrive in infancy</td>
<td>Thick, viscous saliva</td>
<td>Unusual skill with jigsaw puzzles</td>
</tr>
<tr>
<td>Onset of rapid weight gain between ages 12 months and 4 years, causing central obesity</td>
<td>Speech articulation defects</td>
<td>Normal neuromuscular studies (e.g., muscle biopsy, EMG, NCV)</td>
</tr>
</tbody>
</table>

Note: Adapted from Cassidy & Driscoll, 2008; Gurney-Aygun et al., 2001; Holm et al., 1993; Wattendorf & Muenke, 2005.
Prader–Willi syndrome is best known for its symptoms of hyperphagia and obesity, as well as cognitive dysfunction and behavioral weaknesses (Mahgoub, 2007). Prader-Willi syndrome is also characterized by hypothalamic pituitary dysfunction, which contributes to the hyperphagia (Yearwood et al, 2011). Prader-Willi syndrome presents itself with symptoms such as difficulty feeding and failure to thrive in the first year of life (Wattendorf and Muenke, 2005; Cassidy and Schwartz, 2009). Children with Prader-Willi syndrome often have behavioral problems such as temper tantrums, as well as sleep disturbances, skin picking and a high pain threshold (Wattendorf and Muenke 2005). Persons with Prader-Willi syndrome that are obsessive skin pickers tend to have more infected wounds than people who are not obsessive skin pickers (Yearwood et al, 2011). An individual that has Prader-Willi Syndrome will need strict nutritional and dietary supervision in order to reduce the occurrence of obesity and associated problems (Wattendorf and Muenke 2005).

The nutritional intake of individuals with Prader-Willi syndrome have two different phases. From birth until around a year old, poor feeding and failure to thrive occur, while hyperphagia leading to obesity occurs from one year through an individual’s entire life (Lindmark et al, 2010). It is suggested that persons with Prader-Willi syndrome have restricted access to foods, drinks and snacks, while maintaining strict supervision at all times (Lindmark et al, 2010). Individuals with Prader-Willi syndrome have been found to have lower energy expenditure that is a direct result of reduced metabolic rate and low muscle mass (Lindmark et al, 2010). A study performed in Norway examined energy and nutritional intake for children with Prader-Willi syndrome. In general, it was found that children with Prader-Willi syndrome have a reduced consumption of fats, reporting below the recommended fat intake for the population (Lindmark et al, 2010). The study also examined protein intake and found that individuals with
Prader-Willi syndrome had a high intake of protein when compared with total energy intake (Lindmark et al, 2010). People with Prader-Willi syndrome were found to consume the same amount of carbohydrates compared with individuals without Prader-Willi syndrome in the population (Lindmark et al, 2010). The study found that children with Prader-Willi syndrome typically have a 20-40% reduced energy intake compared to the rest of the population (Lindmark et al, 2010). It may be necessary due to reduced intake of essential nutrients that children with Prader-Willi syndrome take supplemental vitamin D, tocopherol iron and calcium (Lindmark et al, 2010).

Infants born with Prader-Willi syndrome will sometimes have decreased fetal movement, have an abnormal position at delivery and an increased risk for cesarean section (Cassidy and Schwartz, 2009; Cassidy and Driscoll, 2009). Infants also show decreased movement, weak cry and poor reflexes during the first few weeks of life (Cassidy and Schwartz, 2009; Cassidy and Driscoll, 2009).

Prader-Willi syndrome often presents in different phases. During the first phase, infants are normally hypotonic with feeding difficulties and failure to thrive (Goldstone et al, 2008). Most infants who are diagnosed with Prader-Willi syndrome have a history of being tube-fed for more than eight weeks as well as a poor sucking reflex (Goldstone et al, 2008). This results in a decreased body weight and body mass index compared to other infants the same age (Goldstone et al, 2008). To help children with Prader-Willi syndrome during infancy, special nipples or feeding devices are used to feed the infant (Cassidy and Schwartz, 2009). During the second phase, children typically gain weight steadily without an increase in caloric intake (Goldstone et al, 2008). Children develop an abnormal interest in food (Goldstone et al, 2008). The third phase is characterized by intense food seeking behaviors and reduced satiety (Goldstone et al, 2008).
During this phase, individuals seem to be hungrier more often. If individuals with Prader-Willi syndrome are given unmonitored access to food, they have the ability to consume three times that of individuals without Prader-Willi syndrome (Goldstone et al., 2008). Phase four shows a decrease in the intense food seeking behavior, although it still remains (Goldstone et al., 2008).

Eighty to one hundred percent of boys who are born with Prader-Willi syndrome have cryptorchidism, or undescended testicles (Goldstone et al., 2008; Cassidy and Schwartz, 2009; Cassidy and Driscoll, 2009). Surgery should be done to move the undescended testicle(s) into place, as there is evidence of hypogonadism and testicular cancer in individuals with Prader-Willi syndrome (Goldstone et al., 2008). About 79% are born with small testes and 69% are born with scrotal hypoplasia (Cassidy and Schwartz, 2009; Cassidy and Driscoll, 2009). Many females with Prader-Willi syndrome are born with labia minora and clitoral hypoplasia (76%), primary amenorrhea (56%) and spontaneous menarche (44%) (Cassidy and Schwartz, 2009). Females also show increased delayed menarche, sometimes not occurring until the person is in their thirties (Cassidy and Driscoll, 2009). In females, oligomenorrhea is also present (Cassidy and Driscoll, 2009). There has also been concern about hygiene issues for females, once monthly menstruation begins (Cassidy and Driscoll, 2009).

In many patients, but not all, hypogonadism is present in both males and females (Goldstone et al., 2008; Yearwood et al., 2011). It is believed that hypogonadism is caused by a failure to secrete normal levels of gonadotropins (Yearwood et al., 2011). Because of this, most persons with hypogonadism and Prader-Willi syndrome will need hormone treatment to initiate and maintain puberty (Goldstone et al., 2008). Females with Prader-Willi syndrome have low Estrogen levels (Goldstone et al., 2008). Male individuals tend to have low testosterone levels (Goldstone et al., 2008).
It is very unlikely for a male or female individual with Prader-Willi syndrome to give birth to a baby (Goldstone et al, 2008). There is a risk of Angelman syndrome in offspring, and mothers with Prader-Willi syndrome suffer from cognitive dysfunction as well as social and emotional immaturity; thus resulting in difficulty caring for a child (Goldstone et al, 2008). Males have reported normal sperm development, however there are no known cases of paternity in Prader-Willi syndrome males (Goldstone et al, 2008).

Individuals with Prader-Willi syndrome also have a severe growth hormone deficiency that leads to their short stature and failure to initiate puberty (Yearwood et al, 2011). Accelerated protein synthesis is caused by a deficiency in growth hormone in Prader-Willi syndrome persons (Yearwood et al, 2011). This can be problematic because protein synthesis causes decreased use of carbohydrates in the body resulting in an increase in fatty-acid metabolism (Yearwood et al, 2011). This only further contributes to the obesity in Prader-Willi syndrome individuals.

Persons with Prader-Willi syndrome often report having other secondary conditions as a result of their primary condition. One secondary condition that is experienced is sleep related breathing disorders (Goldstone et al, 2008). A common sleep related breathing disorder experienced by Prader-Willi syndrome individuals is obstructive sleep apnea syndrome, which is often caused by obesity, kyphoscoliosis and adenotonsillar hypertrophy (Goldstone et al, 2008; Cassidy and Driscoll, 2009). Obstructive sleep apnea syndrome often causes secondary problems itself such as hypertension, cardiovascular disease and cor pulmonale (Goldstone et al, 2008).

Prader-Willi syndrome is also associated with excessive daytime sleepiness and rapid eye movement sleep abnormalities (Goldstone et al, 2008). Daytime sleepiness is thought to be a result of the hypothalamic dysfunction (Yearwood et al, 2011). It is also thought that individuals with Prader-Willi syndrome have a difficult time regulating body temperature (Yearwood et al,
Difficulties regulating body temperature can increase the risk of infection due to the body not being able to respond normally to infections (Yearwood et al., 2011). Persons with Prader-Willi syndrome have reported having a high pain threshold (Yearwood et al., 2011). Orthopedic problems are often experienced in patients with Prader-Willi syndrome (Goldstone et al., 2008). Scoliosis and kyphosis are both found in 30-70% of Prader-Willi syndrome patients (Goldstone et al., 2008). Growth hormone treatment is used to help treat and improve growth/height and body composition (Goldstone et al., 2008). Growth hormone treatment has also been seen to improve muscle tone, increase metabolism, improve respiratory functions, give higher energy levels and increase bone density (Yearwood et al., 2011).

Individuals with Prader-Willi syndrome have reported psychiatric illnesses. Persons with Prader-Willi syndrome often suffer from unpredictable and changing moods, thoughts of suicide, depression and or loss of interest, decreased concentration, decreased or increases in sleep, increased or decreased activity, atypical mental beliefs and experiences (Goldstone et al., 2008). There are reports of obsessive-compulsive characteristics (Cassidy and Schwartz, 2009). Obsessive-compulsive behaviors are found in individuals with Prader-Willi syndrome. These obsessive-compulsive behaviors tend to be “ritualistic behaviors such as hoarding, ordering and arranging objects, insistence on routines, and repetitive speech” (Ho and Dimitropoulos, 2010). To treat psychiatric illnesses, doctors most often use serotonin reuptake inhibitors as well as behavioral therapy (Cassidy and Schwartz, 2009; Cassidy and Driscoll, 2009).

Individuals with Prader-Willi syndrome have intense behavioral problems. Behavioral problems are focused around temper tantrums, stubbornness, controlling and manipulative behavior, compulsive like behaviors, and difficulty adapting to change (Cassidy and Driscoll, 2009; Ho and Dimitropoulos, 2010). It has been thought that many of the behavioral problems
are reflective and similar to that of autism spectrum disorder and attention deficit hyperactivity disorder (Cassidy and Driscoll, 2009, Cassidy and Schwartz, 2009). Autism is believed to have some abnormalities that reside on the same region that Prader-Willi syndrome does, chromosome 15(q11-q13) (Ho and Dimitropoulos, 2010). A correlation has been found between increased body mass index and weight with behavioral problems (Cassidy and Driscoll, 2009).

Almost all children with Prader-Willi syndrome display delayed motor development, such as not sitting up until twelve months and not walking until twenty-four months (Cassidy and Schwartz, 2009; Chen et al, 2010). Children with Prader-Willi syndrome typically have poor speech development, reduced oral motor skills and language deficits (Ho and Dimitropoulos, 2010). Children with Prader-Willi syndrome also have deficits in grammar, narrative abilities and pragmatics (Ho and Dimitropoulos, 2010). Not only are children with Prader-Willi syndrome developmentally delayed, they are also face multiple learning disabilities and most are intellectually challenged. The average IQ range for a child with Prader-Willi syndrome is between 60-70 (Cassidy and Schwartz, 2009; Chen et al, 2010). There is evidence of poor academic performance in children with Prader-Willi syndrome as a result of both developmental delays and intellectual challenges paired with behavioral problems (Cassidy and Driscoll, 2009).

A study was performed to analyze the developmental profiles and mental assessments among children with Prader-Willi syndrome compared to children without Prader-Willi syndrome that were the same age (Chen et al, 2010). The study found that the developmental quotient for children with Prader-Willi syndrome were lower than children without Prader-Willi syndrome (Chen et al, 2010). Expressive language was more impaired in children with Prader-Willi syndrome as well (Chen et al, 2010). Overall, children with Prader-Willi syndrome illustrated uneven global development (Chen et al, 2010).
A recent study comparing individuals with Prader-Willi and individuals with early-onset morbid obesity found that all the individuals with Prader-Willi syndrome had brain abnormalities, whereas the early-onset morbid obesity individuals had none (Cassidy and Schwartz, 2009). Brain abnormalities included ventriculomegaly (100%), decreased volume of brain tissue in the parietal-occipital lobe (50%), sylvan fissure polymicrogyria (60%) and incomplete insular closure (65%) (Cassidy and Schwartz, 2009).

There are several other aspects that affect Prader-Willi syndrome that will be discussed in the following sections. For instance, how specific genes are related to the development of Prader-Willi syndrome will be thoroughly examined. Genetics in relation to the different behavioral characteristics and physical characteristics will also be discussed. Furthermore, growth hormone will be analyzed as a potential treatment option for symptoms associated with Prader-Willi syndrome. Next, the effects of ghrelin and leptin on Prader-Willi syndrome will be explored. Finally, lifestyle adaptations for individuals with Prader-Willi syndrome will be investigated.

Genetics and Prader-Willi

There are an estimated one billion adults on earth who are overweight or obese (Mutch and Clément, 2006). Childhood obesity has increased in the past several years all over the world, especially in the United States (Bouchard, 2009). Over 155 million children and adolescents are overweight, while 40 million are considered obese (Bouchard, 2009). Obesity poses many health implications. Obesity is imminent in adult life if not controlled during childhood (Bouchard, 2009). Secondary conditions to obesity in adulthood are inevitable when obesity is experienced during childhood (Bouchard, 2009). The large number associated with overweight and obesity poses the question of how genetics and environment factors interact to cause obesity (Mutch and Clément, 2006). One genetic classification of obesity is called monogenic obesity, which means
that obesity stems from a naturally occurring dysfunctional gene (Mutch and Clément, 2006). Monogenic obesity cases normally have severe phenotypes and are paired with developmental and sometimes endocrine disorders (Mutch and Clément, 2006). Syndromic obesity is characterized by clinically obese individuals paired with, “mental retardation, dysmorphic features and organ specific abnormalities” (Mutch and Clément, 2006). The most commonly known syndromic obesity disorders include Prader-Willi syndrome, Bardet-Biedl syndrome and Alstrom syndrome (Mutch and Clément, 2006; Butler et al, 2009). As mentioned before, Prader-Willi syndrome is characterized by a deletion of the paternal chromosome 15q11.2-q12 (Mutch and Clément, 2006). Although a gene has been isolated for Prader-Willi, there is still no known gene that causes the hyperphagia in Prader-Willi syndrome individuals (Mutch and Clément, 2006).

The region 15q11.2-q13, where Prader-Willi syndrome occurs, is a highly complex and complicated region that contains many imprinted and non-imprinted genes (Cassidy and Driscoll, 2009). Chromosomes that are homologues are often referred to as interchromosomal, while chromosomes that are separate chromatids of a single chromosome are often referred to as intrachromosomal (Thomas et al, 2006). Paternal deletions of 15q11-q13 cause Prader-Willi syndrome, while maternal deletions of the same chromosome cause Angelman syndrome (Thomas et al, 2006). A study was performed to analyze the specific genetic make up in several genetic deficiency disorders. When analyzing 15q11-q13, an excess of interchromosomal, or chromosomes that are homologues, rearrangements were found (Thomas et al, 2006). Maternal deletions were associated with interchromosomal cases, while paternal deletions were associated with intrachromosomal cases (Thomas et al, 2006). The study also found that the chromosome 15q11-q13 could have a distal breakpoint (Thomas et al, 2006). This breakpoint can be divided
into class/type one and class/type two, depending on where their breakpoints are (Thomas et al., 2006).

There are four different genetic forms of Prader-Willi syndrome (Yearwood et al., 2011). The most prevalent form, about 70% of cases, occurs from deletion of genes from the long arm of chromosome 15 (Yearwood et al., 2011; Bittel et al., 2006; Butler et al., 2009). There are two different types of deletion subgroups, within the most prevalent form of Prader-Willi syndrome, which were addressed briefly previously (maternal and paternal chromosomal deletions). Within these different deletion subgroups, four genes (N1PA1, N1PA2, CYF1P1, and GCP5) have been found to cause compulsive behavior and lower intellectual ability, especially in individuals with Prader-Willi syndrome (Bittel et al., 2006). It has been noted that in T1 deletions, poorer performance is normally seen (Bittel et al., 2006). It was also mentioned that more research is needed to determine if gene expression has a direct influence on behavioral and cognitive characteristic (Bittel et al., 2006). It is known that “a deficiency of the paternally expressed SNORD116 snoRNAs can result in a Prader-Willi syndrome or Prader-Willi syndrome-like phenotype” (Buiting, 2010).

The second form of Prader-Willi syndrome occurs when an individual inherits two copies of chromosome 15 from the mother instead of one from the mother and one from the father, this occurs in about 20% of cases (Yearwood et al., 2011; Butler et al., 2009). This is often called uniparental maternal disomy 15 (Bittel et al., 2006). Individuals with UPD do not show many of the same physical characteristics, or have as severe intellectual disabilities and behavioral characteristics as those without UPD (Cassidy and Driscoll, 2009). However, it is thought that psychological problems and autism like symptoms occur more frequently with UPD (Cassidy and Driscoll, 2009; Yearwood et al., 2011).
Another form, with a prevalence of only 2%-4% of cases occurs from an imprinting defect in the paternal chromosome (Yearwood et al, 2011; Butler et al, 2009). The fourth and last form of Prader-Willi syndrome, which is only found in 1% of cases, occurs when individuals have a structural chromosome rearrangement (Yearwood et al, 2011; Butler et al, 2009). The figures below illustrate how Prader-Willi forms genetically (Buiting, 2010). Figure 3 and 4 describes each of the four different genetic possibilities and how they form based on the most common genetic form of Prader-Willi syndrome (the paternal deletion of chromosome 15q11-q13). Figure 3 and 4 also illustrates how similar Prader-Willi syndrome and Angelman syndrome are genetically.

Figure 3. Prader-Willi Syndrome – Segregation of Imprinting Center Deletions (Buiting, 2010)
As mentioned before, there are four different genetic forms of Prader-Willi syndrome. Most individuals attribute Prader-Willi syndrome to the most common genetic from, the paternal deletion of chromosome 15q11-q13. While all four genetic forms are somewhat different from each other, it is still unknown specific what behavioral and physical implications they present. It is still unknown the exact contributions the aforementioned genes play in the development of Prader-Willi syndrome (Buiting, 2010). There is a need for further research related to genes that affect Prader-Willi syndrome, specifically genes contributing to hyperphagia.

**Ghrelin and Leptin in Prader-Willi Syndrome**

Ghrelin is an orexigenic gastric hormone that is secreted in the duodenum, pancreas, pituitary, hypothalamus, testis, ovary, bone and cartilage (Tan et al, 2004; Choe et al, 2005;
Feigerlová et al, 2008; Hillman et al, 2011). Ghrelin helps to control energy homeostasis by sending signals to the hypothalamic nuclei that control energy homeostasis (Paik et al, 2004; Paik et al, 2007; Hillman et al, 2011). Ghrelin stimulates hunger, which in turn often increases the intake of food causes fat utilization to decrease in humans (Choe et al, 2005; Haqq et al, 2008; Paik et al, 2007). The only substance that is secreted when the stomach empties and is suppressed by eating is Ghrelin is the (Hillman et al, 2011). It has been found that individuals with Prader-Willi syndrome have elevated levels of plasma ghrelin after fasting (Berthold et al, 2007; Tan et al, 2004; Feigerlová et al, 2008; Haqq et al, 2003; Paik et al, 2007). In healthy obese patients there is a negative correlation between body mass index and ghrelin, however this was not observed in children with Prader-Willi syndrome (Berthold et al, 2007). Insulin reduces ghrelin after a meal (Berthold et al, 2007). Persons with Prader-Willi syndrome have a delayed insulin response and a lesser degree of insulin resistance seen in other obese patients without Prader-Willi syndrome (Berthold et al, 2007; Paik et al, 2007).

Leptin is a crucial element in regulating body weight and leptin abnormalities can cause severe obesity (Paik et al, 2004). Children with Prader-Willi syndrome, who are not obese, have been found to have normal levels of leptin concentrations, however plasma leptin levels have been found to be five times higher than children who are not obese (Paik et al, 2004). It is important to understand leptin’s role in the body as many of the studies discussed further below reflect on leptin levels for individuals with Prader-Willi syndrome.

A study was performed to analyze the correlation between fasting plasma ghrelin levels and age, body mass index in individuals with Prader-Willi syndrome (Paik et al, 2004). The results indicate that plasma ghrelin levels in subjects with Prader-Willi syndrome were higher than subjects without Prader-Willi syndrome during a twenty-four hour monitoring period(Paik
et al, 2004). Subjects who had Prader-Willi syndrome, but were not obese showed higher ghrelin levels than subjects who had Prader-Willi syndrome and were obese (Paik et al, 2004). This indicates that as body mass index (BMI) increases, ghrelin levels decrease in subjects with Prader-Willi syndrome (Paik et al, 2004). Fasting ghrelin concentrations were also observed. Children with Prader-Willi syndrome had higher fasting ghrelin concentrations than children who were obese but did not have Prader-Willi syndrome (Paik et al, 2004). The data from the study suggests that the levels of ghrelin in the body are correlated with body mass index (Paik et al, 2004). The study also suggests that the increase in ghrelin secretion for subjects with Prader-Willi syndrome may be due to hyperplasia (or increase) of the cells that secrete ghrelin in the body (Paik et al, 2004). If more cells are secreting ghrelin, this would account for the overall increase in ghrelin secretion. It also suggests that higher levels of ghrelin in the body may cause appetite stimulation through hypothalamic neuuropeptides (Paik et al, 2004).

A different study was performed in children with Prader-Willi syndrome, to investigate the total plasma ghrelin levels at different ages (Feigerlová et al, 2008). Again, plasma ghrelin levels were found to be higher in children with Prader-Willi syndrome than in children without Prader-Willi syndrome (Feigerlová et al, 2008). This particular study also observed two different genetic inheritance differences (paternal deletion and uniparental maternal disomy) and found that there was no difference in plasma levels between these two groups (Feigerlová et al, 2008). The study also found that children with Prader-Willi syndrome with similar ghrelin levels and body mass index experienced an inverse relationship for insulin, HOMA-IR and leptin (Feigerlová et al, 2008). Ghrelin levels were not affected by growth hormone treatment in the present study (Feigerlová et al, 2008). This study produces questions about growth hormone and whether it is effective in the treatment of Prader-Willi syndrome.
A study was performed to determine if children with Prader-Willi syndrome who had high ghrelin levels were also more likely to become obese (Haqq et al, 2008). The data reported that for children with Prader-Willi syndrome, fasting total serum ghrelin levels were higher than in controls, but were not significant (Haqq et al, 2008). The study found that there was more variability in children with Prader-Willi syndrome for serum ghrelin levels than controls (Haqq et al, 2008). This study, like many previous studies, found that plasma ghrelin was elevated in children with Prader-Willi syndrome (Haqq et al, 2008). This study also found that plasma leptin levels were higher in children that had Prader-Willi syndrome compared to controls (Haqq et al, 2008). Older children were observed for a second part of the study. In older children with Prader-Willi syndrome, again fasting serum ghrelin levels were higher in Prader-Willi subjects than controls (Haqq et al, 2008). Similar to the younger children, older children with Prader-Willi syndrome also had an increase in plasma leptin as well as fasting insulin levels (Haqq et al, 2008). The study suggests that during late childhood or early adolescents a relationship develops between ghrelin and weight gain. (Haqq et al, 2008).

An additional study investigated how children with Prader-Willi syndrome and normal children differed in plasma ghrelin and insulin levels compared to the amount of suppression of ghrelin using a specific clamp (Paik et al, 2007). The average insulin level during infusion was not statistically significant for children with Prader-Willi syndrome compared to normal children (Paik et al, 2007). During insulin infusion, the plasma ghrelin level remained stable for both children with Prader-Willi syndrome and normal children, however after insulin infusion stopped, plasma ghrelin levels began to change between the two groups (Paik et al, 2007). The data found that after insulin infusion stopped, children with Prader-Willi syndrome had a higher degree of ghrelin suppression than the normal children, but did not suppress lower than the
normal children’s ghrelin levels (Paik et al, 2007). The study indicated that the “suppression of ghrelin is a result of insulin, not glucose” (Paik et al, 2007). This study highlights that it is important to understand the relationship between ghrelin and insulin, especially in relation to diabetes.

The mucosa from the ileum and large intestine secrete an anorexigenic amino acid peptide called Peptide YY (PYY) (Bizzarri et al, 2010). PYY levels rise after an individual initiates eating and remain elevated for several hours after eating ceases (Bizzarri et al, 2010). A study was performed to “evaluate the potential role of ghrelin and PYY in the hyperphagia of patients with Prader-Willi syndrome” (Bizzarri et al, 2010). Patients with Prader-Willi syndrome have little to no satiety, and high fasting ghrelin levels have been thought to be a contributor (Bizzarri et al, 2010). Children with Prader-Willi syndrome who were treated with recombinant growth hormone on average had lower body mass indexes than body mass indexes for obese patients (Bizzarri et al, 2010). It was also found that ghrelin levels were higher in Prader-Willi syndrome children, however fasting PYY levels were very similar in all subjects (Bizzarri et al, 2010). Results indicated that ghrelin circulating throughout the body changed significantly for children with Prader-Willi syndrome across a span of time (Bizzarri et al, 2010). The results also indicated that children with Prader-Willi syndrome who were treated with growth hormone had higher levels of PYY after a meal (Bizzarri et al, 2010). It was also found that obese children had high glucose levels and insulin levels in comparison to non-obese children. Ghrelin and PYY responses did not change when recombinant growth hormone was administered (Bizzarri et al, 2010). The varying levels of PYY and ghrelin are just one explanation for the hyperphagia in Prader-Willi syndrome patients.

Octreotide is a somatostatin agonist and can be used to treat acromegalic adults and
children that present with obesity related to hypothalamus dysfunction (Hillman et al, 2011). Octreotide has been demonstrated to suppress ghrelin levels significantly (Hillman et al, 2011). Octreotide also decreases plasma ghrelin, and often times decrease insulin and PYY as well (Hillman et al, 2011). A study was performed to determine if lower ghrelin concentrations affects body composition, energy expenditure and growth hormone markers when octreotide administration for 5-7d was administered to children with Prader-Willi syndrome (Haqq et al, 2003). After octreotide treatment plasma ghrelin concentrations decreased (-67%) (Haqq et al, 2003). The study found there to be no leptin or insulin decrease after octreotide administration (Haqq et al, 2003). Additionally, body weight, height and body mass remained the same after octreotide administration (Haqq et al, 2003). Overall, the study found that plasma ghrelin levels to be significantly decreased after short term administration of octreotide (Haqq et al, 2003).

Both acylated and desacetyl ghrelin are present in the stomach (De Waele et al, 2008). A study was performed to analyze fasting and post-glucose plasma acylated and desacetyl ghrelin concentrations in relation to weight gain and food seeking behaviors when octreotide treatment was given for sixteen weeks (De Waele et al, 2008). The study found that there was a negative correlation between total ghrelin and body mass index (De Waele et al, 2008). It was found that octreotide caused a decrease in fasting desacetyl ghrelin and acylated ghrelin concentrations, however it did not effect PYY (De Waele et al, 2008). It was also found that fasting blood glucose increased more with the octreotide treatment than with the placebo treatment phase (De Waele et al, 2008). Octreotide caused a decrease in desacetyl grehlin in five subjects where plasma samples were taken throughout the trial (De Waele et al, 2008). The study also found that there was no octreotide effect on weight or body mass index (De Waele et al, 2008). De Waele et al believed that when ghrelin was suppressed using long acting analogues somatostatin, it would be
possible for the hyperphasia characteristics associated with Prader-Willi syndrome to be treated (De Waele et al, 2008). The experiment found that overtime with octreotide infusions, a decrease (about 60%) was found in total ghrelin concentrations (De Waele et al, 2008). Overall, after sixteen weeks, octreotide treatment was not associated with weight loss (or gain), appetite or food – seeking behaviors in subjects with Prader-Willi syndrome (De Waele et al, 2008).

Ghrelin acts to inhibit insulin secretion and increase glucose levels (Paik et al, 2006). Insulin inhibits ghrelin secretion as well (Paik et al, 2006). One study investigated children with Prader-Willi syndrome and how ghrelin responded to the amount of glucose in the body compared obese children without Prader-Willi syndrome (Paik et al, 2006). The data revealed that fasting glucose levels were not significantly affected in persons with Prader-Willi syndrome (Paik et al, 2006). Acylated ghrelin was found to be higher in subjects with Prader-Willi syndrome than without (Paik et al, 2006). It was also found that desacylated ghrelin was not different for subjects with Prader-Willi syndrome and without Prader-Willi syndrome (Paik et al, 2006). This study supports many other findings that plasma acelated ghrelin is elevated in individuals who have Prader-Willi syndrome (Paik et al, 2006). It was also determined that individuals with Prader-Willi syndrome were insulin sensitive in relation to the total ghrelin (Paik et al, 2006). Overall, the study found that acylated ghrelin is related to insulin sensitivity and that the regulation of acylated ghrelin and desacylated ghrelin are different (Paik et al, 2006).

Somatostatin (a hormone that inhibits the secretion of growth hormone), suppresses ghrelin in non-obese persons (Tan et al, 2004; De Waele et al, 2008). One study focused on the ability of somatostatin to suppress circulating ghrelin levels without reducing appetite in persons with Prader-Willi syndrome (Tan et al, 2004). Data showed that after patients were given a meal,
plasma ghrelin levels were lower in Prader-Willi syndrome subjects if they had been given somatostatin (Tan et al, 2004). Other results indicated that the administration of somatostatin had no effect on the amount of food consumed for persons with Prader-Willi syndrome (Tan et al, 2004). Plasma PYY (an anorexigenic hormone secreted from the intestines) was found to be at equally increased levels for persons with Prader-Willi syndrome who were given somatostatin (Tan et al, 2004). The data also showed that somatostatin had the ability to lower fasting plasma glucose levels before food was administered (Tan et al, 2004). Overall, the data presented indicates that if Prader-Willi syndrome patients are given somatostatin, hyperghrelinemia can be corrected to the same levels seen in obese patients without Prader-Willi syndrome (Tan et al, 2004). Although the results seem promising to the treatment of Prader-Willi syndrome, the intake of food did not change. This suggests that hyperghrelinemia may not be involved directly with hyperphagia (Tan et al, 2004). The present study does suggest that overtime similar therapies may help reduce hyperphagia and obesity in persons that have Prader-Willi syndrome (Tan et al, 2004).

One more study analyzed IGF-I or GH/IGF hyperghrelinemia axis deficiencies (Choe et al, 2005). The study found that not only are plasma ghrelin levels elevated in persons with Prader-Willi syndrome, but also in patients who solely had growth hormone deficiency (Choe et al, 2005). Individuals whom had Prader-Willi syndrome showed more ghrelin expressing cell density compared to patients who were either healthy or obese (Choe et al, 2005). The ghrelin expressing cell densities in the persons with Prader-Willi syndrome also correlated with plasma ghrelin levels in the body (Choe et al, 2005). It was also found that “ghrelin in the gastric body and fundus were quantified by enzyme-linked immunosorbent assay and were found to be significantly higher in persons with Prader-Willi syndrome than in normal obese subjects” (Choe
et al, 2005). Overall, the study found that there were an increased number of ghrelin expressing cells in the subjects who were diagnosed with Prader-Willi syndrome (Choe et al, 2005). This suggests that the elevated plasma ghrelin levels observed in this study, as well as previous studies, may be attributed to the high number of ghrelin expressing cells in the stomach (Choe et al, 2005). The study found that “both Prader-Willi syndrome and growth hormone deficient patients have increased serum ghrelin levels, but only Prader-Willi syndrome patients show an increase in ghrelin expressing cells” (Choe et al, 2005).

As it has been discussed, ghrelin plays a crucial role in Prader-Willi syndrome and obesity. There have been numerous studies on excess ghrelin in relation to patients with and without Prader-Willi syndrome. The relevance of leptin was also discussed. It is crucial that ghrelin and leptin be understood and analyzed to determine the effects on patients with Prader-Willi syndrome and on individuals who are obese.

Growth Hormone and Prader-Willi Syndrome

Many individuals with Prader-Willi syndrome have a short stature because they have little to no growth hormone (Cassidy and Schwartz, 2009). Growth hormone therapy is thought to improve growth rate, body composition, muscle function and energy level (Cassidy and Driscoll, 2009; Paterson and Donaldson, 2003). Many times, if growth hormone treatment is begun early in life, all or many of the physical characteristics of Prader-Willi syndrome are avoidable (Cassidy and Driscoll, 2009). Human growth hormone is approved by the Food and Drug Administration for children with Prader-Willi syndrome (Carrel et al, 2010).

Children with Prader-Willi syndrome have a growth hormone deficiency and therefore, growth hormone is given as a treatment to these children (Berthold et al, 2007). Growth hormone treatment is suggested for a short-term period, but is not recommended for long-term use
There is evidence that short-term growth hormone administration improves short stature and growth, as well as puberty in patients with Prader-Willi syndrome (Paterson and Donaldson, 2003). Similarly, muscle tone and strength, as well as exercise tolerance and development of gross motor skills also improved with growth hormone therapy (Paterson and Donaldson, 2003).

A study was performed to figure out what the “influence of growth hormone was on acylated and total ghrelin concentrations before and after oral glucose load, and on insulin resistance” in children with Prader-Willi syndrome (Berthold et al, 2007). Ghrelin, or acylated ghrelin, is an amino acid produced in the stomach. Plasma ghrelin is the amount of ghrelin found in the blood. No growth hormone decrease was observed for acylated ghrelin either before or after administration (Berthold et al, 2007). After administration of carbohydrates, both plasma total ghrelin and acylated ghrelin levels decreased in children with Prader-Willi syndrome (Berthold et al, 2007). Glucose levels remained normal during all points of the study for Prader-Willi syndrome patients (Berthold et al, 2007). In the current study, Prader-Willi syndrome patients were found to have increased body fat to total body weight, decreased ratio of visceral to total adipose tissue, a not as strong insulin resistance and severely elevated total ghrelin and acylated ghrelin concentrations (Berthold et al, 2007). The present study found that growth hormone treatment was successful at decreasing elevated basal and post carbohydrate total ghrelin concentrations in children and adolescents with Prader-Willi syndrome (Berthold et al, 2007). It was found that acylated ghrelin was not changed by growth hormone treatment in the present study (Berthold et al, 2007).

Magnetic resonance imaging shows that the posterior pituitary bright spot is absent or very small, showing a flaw in the hypothalamus (Paterson and Donaldson, 2003). A pituitary
bright spot is when small granules of antidiuretic hormone are present in the pituitary gland. It is known that obesity in children shows spontaneous growth hormone levels to be impaired, even though growth factor levels are normal (Paterson and Donaldson, 2003). Impaired hypothalamopituitary secretion of growth hormone is demonstrated through impaired growth responses and low growth factor levels (Paterson and Donaldson, 2003).

A study was performed to analyze the effect of human growth hormone over a period of six years on children with Prader-Willi syndrome (Carrel et al, 2010) Individuals with Prader-Willi syndrome who were treated with human growth hormone had a lower body fat percentage than those who were not treated with human growth hormone (Carrel et al, 2010). Muscle mass was also greater in children with Prader-Willi syndrome who received the human growth hormone treatment than in those that did not (Carrel et al, 2010). Cholesterol levels were significantly lower in children with Prader-Willi syndrome who were treated with human growth hormone compared to those who were not treated (Carrel et al, 2010). Glucose remained unaffected for both groups in the study (Carrel et al, 2010). In addition to all the nutritional findings, improved motor function strength was observed in children with Prader-Willi syndrome who were treated with human growth hormone (Carrel et al, 2010). The findings of this study show that early treatment with human growth hormone significantly improve health implications brought on naturally by Prader-Willi syndrome.

Nutrition and Food Seeking Behaviors in Prader-Willi Syndrome

Children with disabilities were found to be more likely to not eat breakfast during the week (Neter et al, 2011). It was also found that disabled children tended to consume significantly more sugary drinks during the week than nondisabled children (Neter et al, 2011). Individuals with Prader-Willi syndrome have been found to have lower energy expenditure that is a direct
result of reduced metabolic rate and low muscle mass (Lindmark et al, 2010). It may be necessary due to reduced intake of essential nutrients that children with Prader-Willi syndrome take supplemental vitamin D, tocopherol iron and calcium (Lindmark et al, 2010). Individuals with Prader-Willi syndrome that had a lower body mass index and weight on average had more psychological problems than those who had higher body mass index and weights, therefore it is suggested to not place a Prader-Willi syndrome individual on a strict caloric diet Yearwood et al, 2011).

During infancy, focus needs to be placed on making sure the infant receives enough nutrition through supplemental feeding techniques. (Cassidy and Driscoll, 2009). It is suggested that a regular feeding schedule be established (Cassidy and Driscoll, 2009).

A study was conducted on adolescent individuals with Prader-Willi syndrome. Individuals were placed on a special diet consisting of 25% proteins, 20% fat and 55% modified carbohydrates (Bonfig et al, 2009). Body mass index was found to decrease significantly ($p < .01$) after one year (Bonfig et al, 2009). Results also indicated that after two years, body mass index remained significantly ($p < .01$) lower than when the study was started (Bonfig et al, 2009). In a follow up study, the diet was found to still be producing weight stabilization after four to six years (Bonfig et al, 2009). It was noted that subjects did not continue losing weight after the first year, but did continue to maintain the same weight (Bonfig et al, 2009).

An individual that has Prader-Willi Syndrome will need strict nutritional and dietary supervision in order to reduce the occurrence of obesity and associated problems (Wattendorf and Muenke 2005; Cassidy and Driscoll, 2009). Persons with Prader-Willi syndrome are suggested to have restricted access to foods, drinks and snacks, while maintaining strict supervision at all times (Lindmark et al, 2010). It is suggested that foods high in carbohydrates
and fat should not be kept within reach of Prader-Willi patients as they have been known to hoard and devour food in abnormal quantities (Yearwood et al, 2011). Persons with Prader-Willi syndrome participate in hoarding foods as well as eating inedible objects (Cassidy and Schwartz, 2009; Cassidy and Driscoll, 2009). Often times Prader-Willi, persons will steal money to buy food (Cassidy and Schwartz, 2009; Cassidy and Driscoll, 2009). Individuals with Prader-Willi syndrome may be incapable of making decisions based on eating. This requires daily management and control of foods under lock and key to keep individuals from eating themselves to death (Ho and Dimitropoulos, 2010).

![Figure 5. General Linear Model of Food Activation in Control Subjects and Prader-Willi Syndrome Subjects (Miller et al, 2007).](image)

Brain imaging in figure five above shows that Prader-Willi syndrome individuals show an increased activity in the prefrontal cortex when viewing pictures of food following glucose administration (Miller et al, 2007). Researchers found this to be consistent with a intense “reward
response to food in Prader-Willi syndrome individuals” (Miller et al, 2007). It should also be noted that the frontal cortex is associated with emotion, stimulus – reinforcement association learning. In further studies, the fusiform gyrus and the parahippocampal gyrus should be studied to see if the same effects are seen.

As mentioned previously, individuals with Prader-Willi syndrome are more likely to not eat breakfast and more likely to consume sugary drinks and eat more unhealthy than individuals without Prader-Willi syndrome. It was also noted that individuals with Prader-Willi syndrome should not be placed on a strict caloric diet as there was a correlation with low body mass index and psychological problems in patients with Prader-Willi syndrome. Children with Prader-Willi syndrome are suggested to be placed on a strict diet so that they do not have free access to foods, as this can be dangerous. It should also be noted that children with Prader-Willi syndrome should be closely watched as to not hoard and hide food for later consumption. Individuals with Prader-Willi syndrome need lots of guidance and education related to nutrition and how to regulate meal intakes,

Conclusion

There is a need to focus research on how to teach disabled children healthy eating decisions and to change risk behavior in disabled children (Neter et al, 2011). The primary focus on treatment of Prader-Willi syndrome should be placed on weight control (Yearwood et al, 2011). An individual that has Prader-Willi Syndrome will need strict nutritional and dietary supervision in order to reduce the occurrence of obesity and associated problems (Wattendorf and Muenke 2005). It has been found that children with Prader-Willi syndrome have uneven global developmental delay (Chen et al, 2010). It was also found that children with Prader-Willi syndrome have better fine motor ability than gross motor ability (Chen et al, 2010). Children
with Prader-Willi syndrome will need to work with a variety of specialists during their lifetime. It is important because of developmental delays that children with Prader-Willi syndrome work with physical therapists, occupational therapists and speech therapists (Cassidy and Driscoll, 2009). It is also important that children with Prader-Willi syndrome have an individualized education plan and individualized appropriate education (Cassidy and Driscoll, 2009; Cassidy and Schwartz, 2009). Persons with Prader-Willi syndrome have difficulty relating to others in a social setting. They have tendencies to be impulsive and react poorly to change, as well as lack the ability to filter social cues (Yearwood et al, 2011).

There is no cure for Prader-Willi syndrome, only proactive approaches and treatments to make life more enjoyable for those with the syndrome (Ho and Dimitropoulos, 2010). As mentioned before, growth hormone treatment can be used to help with the symptoms and conditions associated with Prader-Willi syndrome, but will not be able to cure this genetic disorder. Bariatric surgery has not proved to be effective in the treatment of Prader-Willi syndrome (Ho and Dimitropoulos, 2010). Appetite suppressants, or antiabsorptive agents have been found ineffective in the treatment of Prader-Willi syndrome (Bonfig et al, 2009). Individuals with Prader-Willi syndrome who do have normal body proportions are more likely to be physically active, which is another important factor for weight control. In general tailored exercise programs three to five times weekly are recommended for patients with Prader-Willi syndrome” (Bonfig et al, 2009).

Finally, families can experience lots of stress and anxiety depending on the extent of emotional and behavioral problems when they have a family member with Prader-Willi syndrome (Ho and Dimitropoulos, 2010). A multidisciplinary team is needed in the treatment of Prader-Willi syndrome over the course of an individual’s life. Death from Prader-Willi syndrome
normally occurs from complications of obesity such as cardiovascular problems and respiratory problems (Cassidy and Driscoll, 2009). Some have reported that individuals with Prader-Willi syndrome rarely live beyond thirty years of age due to secondary complications. (Paik et al, 2007).

In conclusion, Prader-Willi syndrome occurs in about 1/25,000 live births and causes hyperphagia, obesity, developmental disabilities and intellectual disabilities. Persons with Prader-Willi syndrome have been known to have psychiatric disorders, specifically depression. An individual with Prader-Will syndrome will struggle with food intake regulation throughout life. It is not uncommon for individuals with Prader-Willi syndrome to steal or hoard food to fulfill their food seeking desires. Treatment for Prader-Willi syndrome occurs over the course of an individual’s life and is always adapting to better accommodate needs of the individual with Prader-Willi syndrome.
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