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# Issues in Adults Prader-Willi Syndrome

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Prader-Willi syndrome (PWS), a complex genetic disorder, arises from suppressed expression of paternally inherited imprinted genes on chromosome 15q11-q13. Characteristics include short stature, intellectual disability, behavioral problems, hypogonadism, obesity, and reduced bone and muscle. The life expectancy of persons with PWS has increased in recent years. Cardiovascular diseases, diabetes, dermatological, and orthopedic problems are common physical complaints in older people with PWS. Behavioral problems are major concerns in adults with PWS into old age. And aging is also associated with significant social and economic changes. Age-related physical morbidity, physical appearance, behavioral and psychiatric problems, functional decline and economic problems can be combined in older PWS. The care for older people with PWS requires a life span approach that recognizes the presence, progression, and consequences of specific morbidity.

**Keywords:** Prader–Willi syndrome, Health, Life expectancy, Behavior

## Introduction

Prader-Willi syndrome (PWS) is a contiguous gene syndrome caused by the non-expression of the paternal alleles in the PWS region of chromosome 15q11e13[1)]. PWS is the single most common known genetic cause of obesity with an estimated population prevalence varying from 1:49,911 up to 1:91,802[1)].The clinical picture of PWS includes muscular hypotonicity, early childhood-onset obesity, characteristic appearance, hypogonadism, impaired growth hormone secretion, mild or severe mental retardation, and behavioral disturbance[2)]. Some of the typical features of PWS seem to reflect a hypothalamic dysfunction[3)]. In the early period of life, PWS is characterized by severe neonatal hypotonia, feeding problems and a failure to thrive. In absence of intervention, weight excess typically begins after 2e3 years of age and is later exacerbated by hyperphagia with lack of satiety. Consequently, a disproportionate accumulation of body fat develops as early as in childhood[4)] and leads progressively to severe obesity by the adult age[2)]. The average age of people with Prader-Willi syndrome (PWS) is likely to increase but research on PWS has mainly focused on clinical characteristics in child- and early adulthood and little is known about PWS at older age. Until recently, survival past the 5th or 6th decade was thought to be very unusual for persons with PWS. It was estimated that the mortality rate of people with PWS was 3% per year across all ages, rising to 7% in those aged over 30 and high morbidity in adults with PWS results in high mortality rates and a lower life expectancy than the general population[5)].

Because of the lack of reports on older persons with PWS, the natural history, onset, and type of age-related problems are not well known. However, it is important because knowledge of the age-related health risk factors can lead to enhanced prevention or early diagnosis of the impaired conditions and thus may lead to improved quality of life of those concerned.

## Issues in General Health

Generally, aging in people with intellectual disabilities, comes together with physical and mental changes[6)]. Many of the changes are not caused by the aging process, but by disease, the environ-

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ment, and lifestyles[7]. Some of the changes caused by these factors may be prevented or slowed down by taking action. Caregivers should be provided with ongoing information regarding healthy living, such as nutrition, oral hygiene, and substance abuse[8].

People who live an inactive lifestyle lose muscle mass and may gain weight as they age. In PWS it is particularly important to maintain mobility into older age. Healthcare providers for older adults with PWS should be aware that adult (and older) age onset medical conditions are common in this population[9]. Regular surveillance of health (e.g., following a checklist as proposed by Sinnema et al.[10] is recommended in this population. Physicians should be alert for the presence of cardiovascular diseases, diabetes, dermatological, and orthopedic problems. And sleep problems and osteoporosis are likely to be underreported and deserve special attention. The combination of temperature instability, the reduced ability to vomit, and a high pain threshold is typical for PWS and may mask the initial symptoms of illness[11].

In case of unexplained serious illness, a respiratory infection should be ruled out. The diagnosis of pneumonia is frequently delayed in older adults with PWS because of the absence of fever and the course can be very detrimental. And low body temperature (e.g., after swimming), anemia, diabetic dysregulation, and adverse reactions to medications should also be considered in case of medical problems in older people with PWS[9].

Presently, there is no research to suggest that preventative health practices that are recommended for the general population, throughout the lifespan, should be with held from people with PWS[7]. Therefore, age appropriate screening protocols for conditions, such as sensory impairment and various forms of cancer (with the possible exception of PAP smears in women without a history of sexual activity), should also be offered to adults with PWS[9].

Growth hormone therapy might also have positive effects on functional decline and energy levels of older people with PWS[12]. Staff should be provided with knowledge on syndrome-specific age related characteristics and should be trained on how to integrate this in existing practices[9].

## Issues in Behavior and Psychiatry

Behavioral problems are significant in PWS and include: repetitive, compulsive behaviors; insistence on sameness; tantrums or outbursts (especially with changes in routine); skin-picking; food-seeking; aggression and tantrums; irritability; emotional lability, and hoarding[11]. The trajectories of these behavior problems in adulthood remain unclear. Some persist or even worsen in adulthood, especially hoarding and collecting non-food items, skin-picking, irritability, food-seeking and mood swings[13]. Dykens noted a peak of externalizing behavior problems (e.g., aggression, impulsivity) in young adulthood, with fewer such behaviors in older adults aged 40 and higher[14].

Sinnema et al. show that behavioral problems are major concerns in adults with PWS into old age. They found most behavioral problems in adults with the mUPD subtype. In contrast, other studies reported that persons with a mUPD have less skin picking and maladaptive behavior than persons with a deletion[15]. but heightened vulnerabilities in young adulthood for psychiatric disorders, such as atypical psychosis and affective disorders[16]. Increased rates of psychosis in mUPD are thought to relate to the overexpression of maternally imprinted genes in this genetic subtype. Longitudinal studies of these psychiatric concerns have yet to be published, leaving it unknown if they remit with early treatment, reemerge at stressful times, or contribute to ill health later in adulthood[17].

Psychiatric symptoms usually started at young adult age and had a cycloid course through adulthood[16,18,19]. The chronic course of psychiatric illness and chronic use of psychotropic medication might have effects on the aging process in PWS. For instance, changes in cognitive performance and functional outcomes have been reported in late life in people from the general population with schizophrenia[20] and people with 22q11 deletion syndrome and psychiatric problems[21]. Many in the older group (8/12) with PWS used more than one different psychotropic medications. Adverse effects to medication, and especially psychotropic medications, are frequently reported in PWS[18,22]. Sensitivity to psychotropic medication differs with age[23] Therefore, it is important to reassess the need for and dosage of psychotropic medication in older people with PWS, in order to find the lowest possible effective dose as well as minimal side effects[24]. The association between PWS and dementia could of course be coincidental. Nevertheless, in order to achieve a better understanding of the prevalence of dementia in older people with PWS, more studies are necessary[10].

Weight loss in adulthood may be associated with improved physical health but not necessarily mental health. Relative to overweight or obese adults, those with lower BMIs show more distress, tearfulness, confusion, restlessness, screaming, excitation, repetitive movements, and anxiety[10,14]. These findings may relate to hormonal changes or to the inherent stress of maintaining weight loss and a low calorie diet when one is "always hungry, never full" (National Prader-Willi Syndrome Association motto).

## Issues in Social-Economic Changes

Aging is also associated with significant social and economic changes. In older adults it is important to recognize when lifestyle should be changed (e.g., less time at work or day care center) or retirement should be planned[25]. Increasing age for people with PWS is also associated with the aging and death of family members. Bereavement is frequently associated with behavioral disturbances and emotional distress[26]. Therefore, caregivers should acknowledge the need for emotional support when family circumstances change. The loss of family members may also mean that important information about a person's (medical) past and the family is lost. Life story books are a way of trying to maintain at least some of this knowledge[27].

Although many adults coreside with their parents, dedicated Prader-Willi syndrome group homes have been very successful in helping individuals lose weight and gain social and coping skills. Almost all adults need psychiatric or behavioral interventions, reduced calorie diets, supervision around food, and daily physical activity or exercise[17]. Employment for adults is hard because employers need to provide food supervision or a food secure work environment. More so than others with disabilities, both men and women with Prader-Willi syndrome seem drawn to taking care of pets or children. This desire to care take may relate to aberrant plasma or CSF levels of levels oxytocin[28].

Adults with Prader-Willi syndrome also gravitate to word find and jigsaw puzzles, and many perform them quite proficiently, on par or exceeding chronological agematched controls[29]. Recreational use of electronic or computer games may confer some cognitive advantage to adults, but increased computer or TV screen time is also associated with higher BMIs in adults with Prader-Willi syndrome[29].

## Conclusion

As more increasing people with PWS, it is important to understand that morbidity and mortality may result from the consequences of early age onset conditions, through their long-term progression or their interactions with older age onset conditions. It is required that corresponding increase in training and preparation of physicians and other healthcare professionals for older people with PWS. Consequently, regularly scheduled preventive management following practical guidelines is needed. Longitudinal studies are needed, because of the recognition that age-related health problems of later life stages are particularly significant for older people with PWS.

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