the Child Dental Patient with

Prader-Willi Syndrome

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European Reference Network
for rare or low prevalence complex diseases
Network
Craniofacial anomalies and ear, nose and throat disorders (ERN CRANIO)
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Definition

- Prader-Willi syndrome (PWS) is a complex multisystemic genetic disorder caused by the lack of expression of certain paternal genes located on the chromosome 15q11-q13.
- This anomaly causes cognitive, neurological and endocrine abnormalities, among which one of the most important is hyperphagia.
- Prader-Willi syndrome includes also craniofacial and dental anomalies.
- PWS is characterized by two stages:
  - Newborns present severe hypotonia, global developmental delay and lack of appetite, thus difficulty gaining weight, and in most cases, feeding *via* nasogastric tube is necessary.
  - The second stage begins during early childhood; it is characterized by an eating disorder known as hyperphagia, which favors overweight and obesity.

www.orphanet.fr

Epidemiology

- Prevalence at birth is estimated at 1/15 000 to 25 000 worldwide (3.1: 100 000 live newborns in Europe)
- The syndrome affects both males and females equally.

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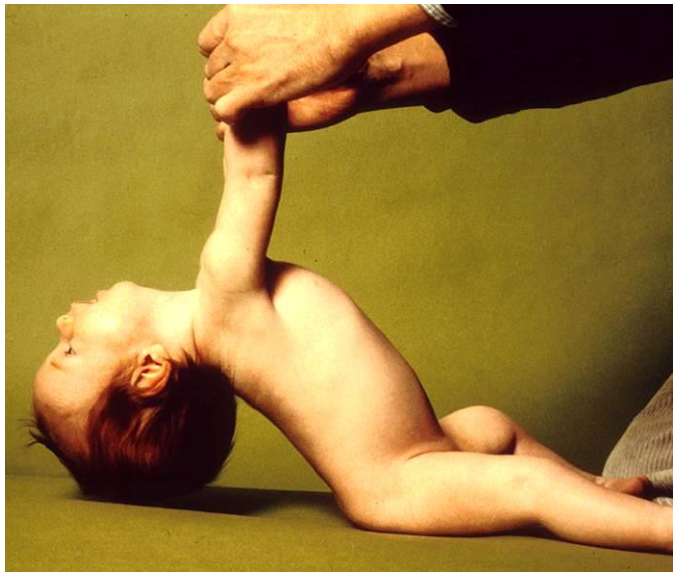
Etiology and diagnosis

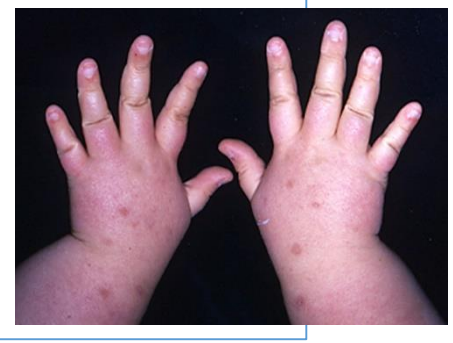
- The disease is clinically and genetically heterogeneous. Frequently it is caused by either a paternally derived 15q11-q13 deletion, maternal disomy or, very rarely, imprinting defects in the same region.
- PWS should be suspected on the presentation of **severe neonatal hypotonia**, and confirmed by genetic testing.
- **Differential diagnosis**
  - At birth, genetic testing should be used to exclude other causes of hypotonia. If the neonatal phenotype evokes PWS and the genetics are negative, genes for the Prader-Willi-like syndrome (PWS-like) should be searched.
  - In older individuals, the differential diagnosis is of other syndromic obesities such as Bardet-Biedl syndrome, Alström syndrome and, particularly, PWS-like.
  - Most cases are sporadic; however, in rare cases dominant transmission may occur with 50% risk where the father carries the imprinting defect.



Clinical description: hypotonia, obesity, endocrine disorders

- The **severe hypotonia** at birth is associated with poor oral and social skills which remain throughout life.
- After this initial phase, followed by an excessive weight gain without changes in eating, the most striking signs appear: **hyperphagia and absence of satiety** often leading to **severe obesity** in affected children as young as three years of age. The situation may deteriorate quickly without strict control of food access.
- Associated comorbidities may include type II diabetes, hepatomegaly, gastrointestinal problems, and infections.
- Spinal deformities include scoliosis, kyphosis or kyphoscoliosis, and are present in about 40%

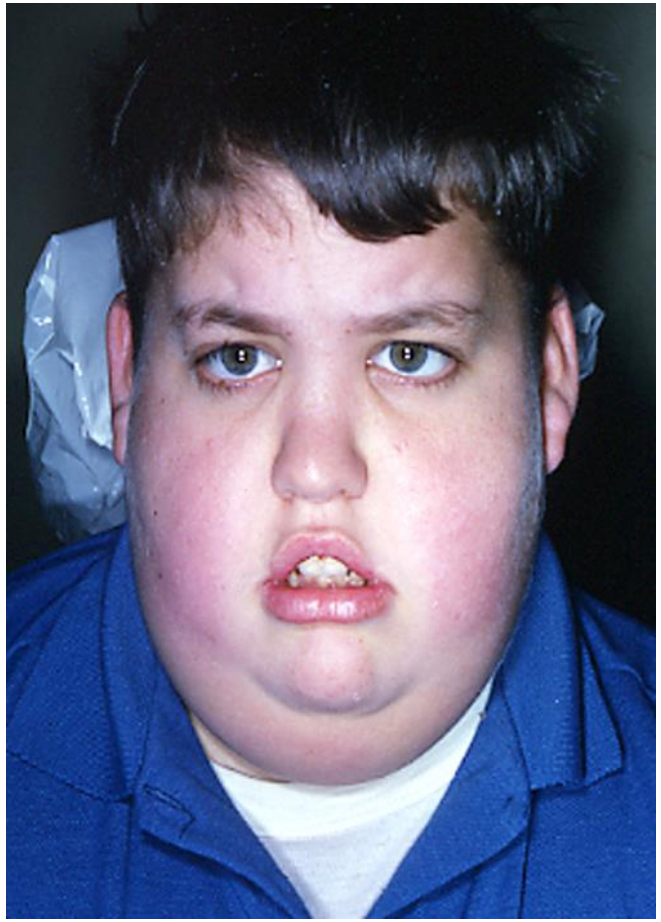
- Other associated endocrine abnormalities include:
  - short stature due to a growth hormone (GH) deficiency
  - incomplete pubertal development due to hypogonadism of mixed (central and peripheral) origin
  - hypothyroidism
  - premature pubarche.
- Hypothalamic alterations can cause:
  - intellectual disability
  - behavioral problems
  - thermoregulatory dysfunction
  - a high pain threshold
  - respiratory sleep disorders
  - hypopigmentation
  - hypogonadism
  - pubertal delay and infertility
  - short stature, and small hands and feet.



"Children with PWS gradually show increased interest in food and weight gain from 2 years of age that is inevitably followed by a strong and uncontrollable, biologically- determined drive to seek and eat food"

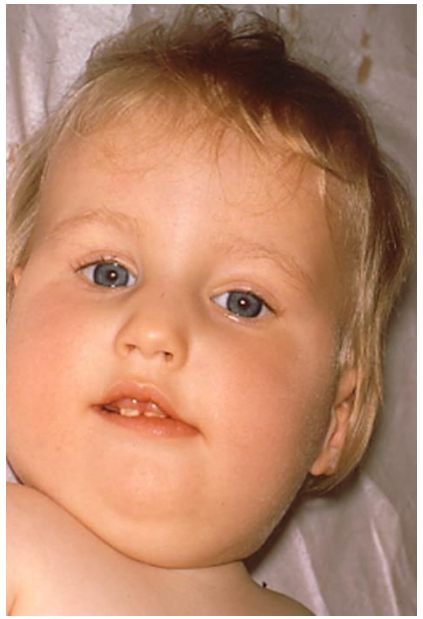
Clinical description: cognitive impairment

- The degree of cognitive dysfunction varies widely but is mild/moderate in most of the individuals.
- It is associated with :
  - learning disabilities
  - impaired speech and language development
  - aggravated further by psychological and behavioral troubles, impaired social abilities, and control of emotions.
  - poorer Quality of Life scores



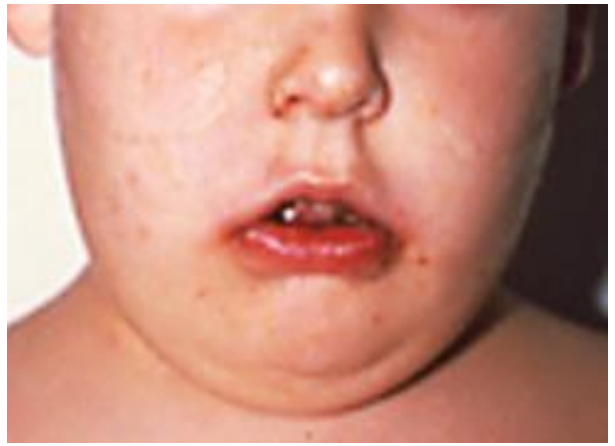
Clinical description: oro-facial features

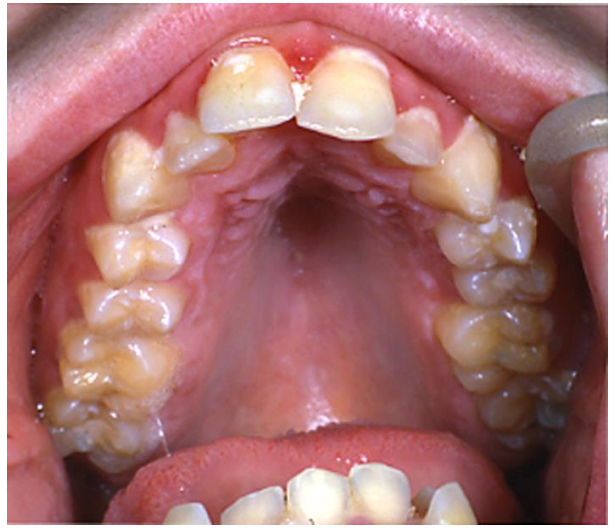
- Characteristic facial features:
  - a narrow forehead
  - almond-shaped eyes
  - a triangular mouth with commissures facing downwards and thin upper lip
  - varying degrees of oral motor dysfunction is common.



Oro-dental pathologies

- The dietary problems associated with this general systemic condition **increase the risk of oral diseases**.
- Pediatric patients with PWS are at greater risk of suffering oral pathologies such as:
  - dental caries: combination of the lack of oral hygiene, reduced salivary flow, mouthbreathing and the preference for foods high in carbohydrates
  - extensive tooth wear caused by attrition, erosion (gastric reflux, acid food) or abrasion
  - periodontal diseases
  - delayed tooth eruption
  - candidiasis or other oral lesions
  - decreased salivary flow and more acidic salivary pH
  - malocclusions.
- The frequency of enamel hypoplasia is now lower as an optimal feeding is initiated during early infancy. *Saeves et al* noted a higher prevalence of hypodontia in PWS patients compared to control group.
- The **low salivary quantity and quality** could be due to atrophy of the salivary glands, which in turn is due to the low birth weight. Increased amounts of salivary ions and proteins make the saliva sticky, sparse and unable to perform its functions.
- These alterations may be aggravated by the hypotonia which hinders suction, swallowing and chewing and makes the introduction of a soft diet mandatory.





Saliva study

	GROUP	n	Mean	SD	*P* value
ml/min	PWS	18	0.475	0.5714	0.032
	Control	25	0.848	0.4932	
pH	PWS	27	6.15	0.818	0.0001
	Control	30	7.53	0.776	
DMFT	PWS	30	2.5	3.170	0.017
	Control	30	0.93	1.311	

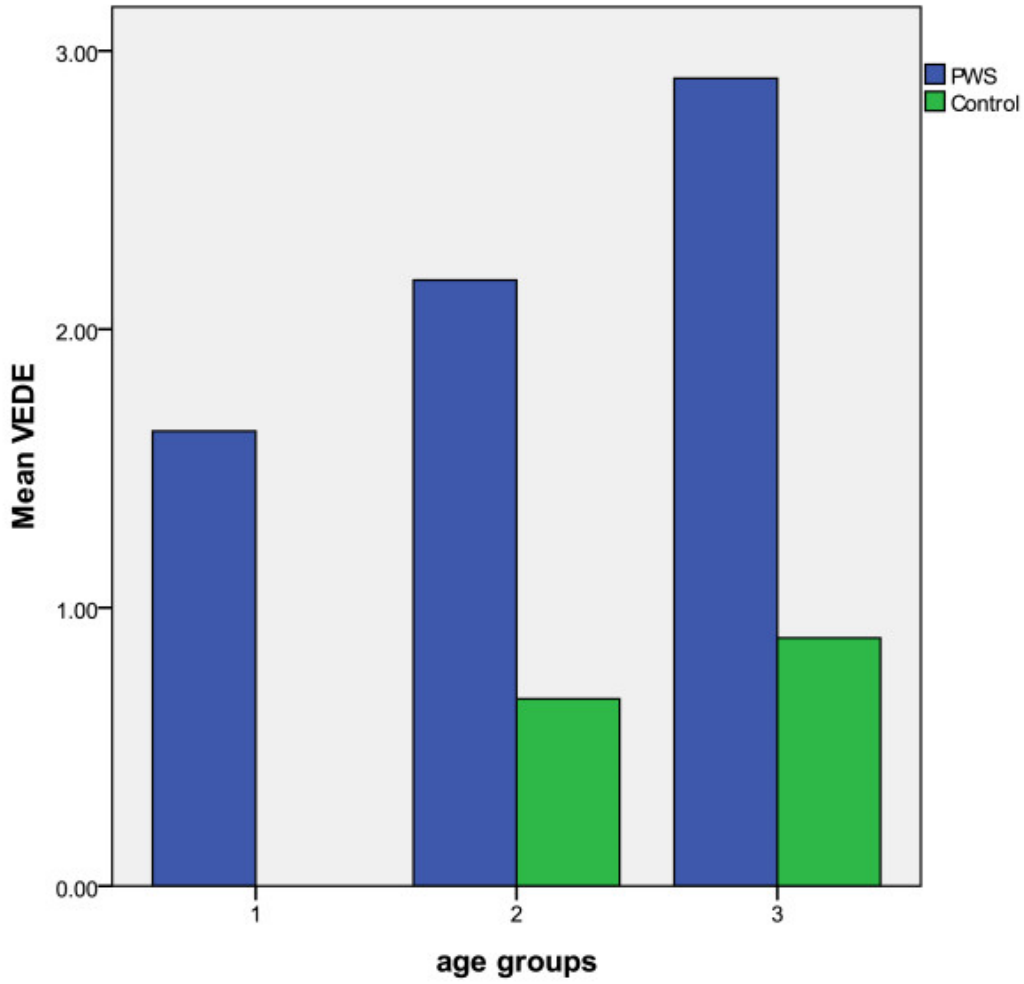
Comparison of stimulated salivary flow, pH and DMFT in two populations PWS and control (Munné-Miralvés, Orphanet J Rare Dis, 2020)

$p < 0.05$. Student *t*-test

Severe tooth wear in Prader-Willi syndrome. A case–control study

Tooth wear was correlated significantly with age and saliva secretion.

Tooth grinding was significantly associated with tooth wear and could explain it to some extent.



Tooth wear presented as mean VEDE for individuals in PWS- and control-group divided in three equally large age groups. Age groups (mean age, range years): 1; 9.8 (6.1-13.6) (n = 32), 2; 20.2 (13.7-25.4) (n = 34), 3; 31.5 (25.5-42.5) (n = 32).

Saeves et al, BMC Oral Health, 2012

Medical management and prognosis

Multidisciplinary management should be implemented very early, with particular attention paid to families with psychosocial difficulties. Principally:

- **a strict control of food access** : calorie restriction and careful monitoring to prevent obesity while maintaining a nutritionally balanced intake with adequate protein and fats
- **exercise program**
- sensory motor stimulation
- psychology - speech and language therapy
- growth hormone (GH) treatment to stabilize body mass index, improve linear growth and adult height
- associated comorbidities require systematic screening and evaluation (ex: polysomnography for assesment of sleep pathology; scoliosis treated with bracing and may require surgery).
- Currently, there are no approved medications to specifically improve the behavioral problems or degree of autonomy obtained. Clinical trials are ongoing for various drugs targeting hyperphagia and behavior.

Prognosis

- **obesity** is a major factor influencing morbidity and mortality
- early diagnosis, early multidisciplinary care and GH treatment have greatly improved the quality of life of affected children
- in children, treatment with GH before 1 year of age improves cognitive development
- adolescents benefit from continuing GH treatment
- adults who have received GH as children have lower BMI and less comorbidities.
- autonomies can be reached but **not complete autonomy**.

Dental management

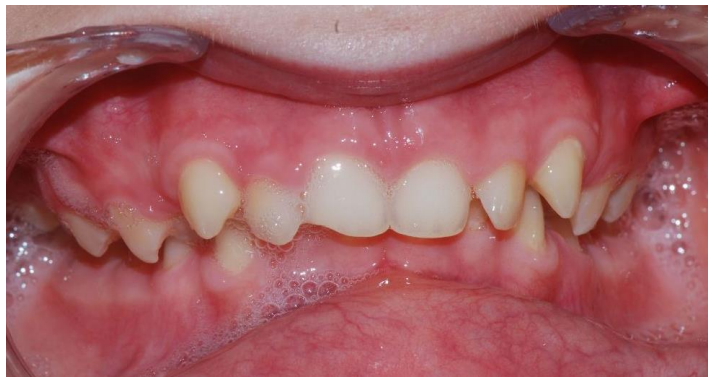
Prevention

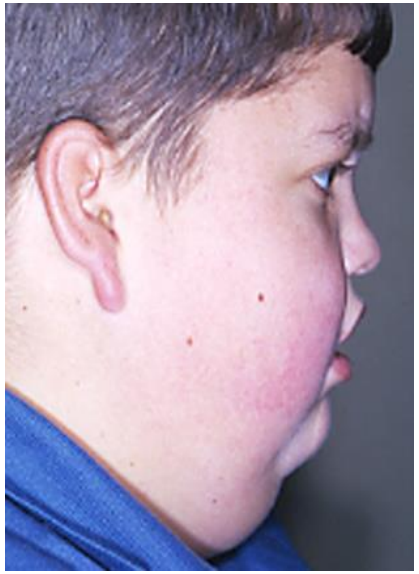
- First dental visit as early as possible (between 9 and 18 months of age):
  - thorough clinical history
  - assessment of oral diseases and of caries risk
  - evaluation of ability to cooperate.
- Observation of basic prevention guidelines from the first year of life:
  - good levels of oral hygiene: usually poor as many children do not permit parents or guardians to help them for toothbrushing
  - application of topical fluoride gels or daily rinses could be recommended
  - low sugar diet
  - reducing dietary consumption of acid and replacing soft drinks with water to also protect against tooth wear
  - frequent preventive dental appointments.

Dental management

Dental care

- High pain threshold in individuals with PWS should be taken into account in the examination and treatment of these patients (*They may not be able to locate the site of discomfort*). Behavioural and cognitive issues have also to be taken in account.
- Dental procedures under local anesthesia are possible.
- Use of mouth openers could be helpful (patients' poor muscle control, fatigability)
- Tooth wear management :
  - closely monitored
  - dental splints may be useful for some patients, but poorly-tolerated by others
  - restorative and prosthodontic rehabilitation could be indicated.
- Orthodontic management:
  - mouthbreathing
  - obtructive sleep apneoa
- Xylitol chewing gums or saliva substitutes indicated in some cases.





If the child is treated in an hospital setting, it is important to coordinate the appointments with different specialists on a single day, so as not to disrupt families' daily routines and to avoid multiple hospital visits.

Conclusion

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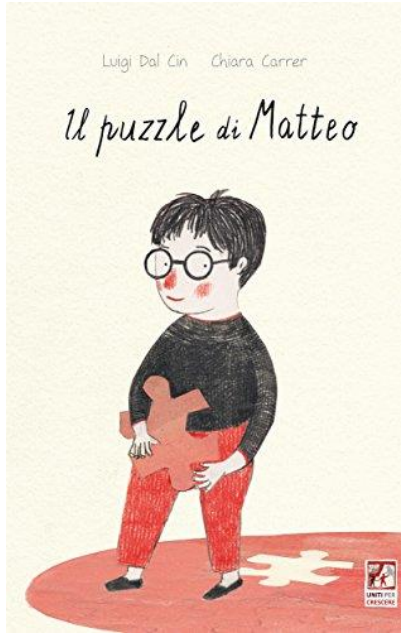
- It is a complex condition requiring a complex management, constant care and which poses multiple challenges.
- Dental care is an essential part of the multidisciplinary therapeutic approach of children with PWS.
- Establishing a dental prevention protocol at very early stages of life is essential.
- Being in contact with a parents' association is very helpful for dental management.

Prader-Willi France



La sindrome di Prader Willi raccontata ai bambini

https://www.prader-willi.fr
www.prader-willi-guide.fr

www.orphanet.fr

Le syndrome de Prader-Willi Encyclopédie Orphanet Grand Public 36www.orpha.net/data/patho/Pub/fr/PraderWilli-FRfrPub139.pdf

IPWSO International Prader-Willi Syndrome Organisation

http://www.ipwso.org.

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