MRC Cognition and Brain Sciences Unit
75th ANNIVERSARY 1944 - 2019
UNIVERSITY OF CAMBRIDGE

NHS
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Prader-Willi Syndrome:
clinical presentations and genetic diagnosis

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IPWSO HEALTH ECHO 16th Feb 2021

Outline

Information

1. Clinical characteristics of PWS across the lifespan
2. Genetic basis of PWS
3. Diagnostic genetic testing

Objectives

1. Recognise a person who might have PWS
2. Awareness of diagnostic testing pathway

What is Prader Willi Syndrome (PWS)?

- Lifelong, multi-system condition affecting physical and mental health
- Loss of gene expression from paternal copy of chr 15q11–13
- ~ 1/10,000 to 1/30,000 liveborn incidence
- Core shared characteristics, but every person is unique
- Although there is no “cure”, physical and mental health outcomes can be greatly improved via early diagnosis and optimal management

PWS across the lifespan

Prenatal

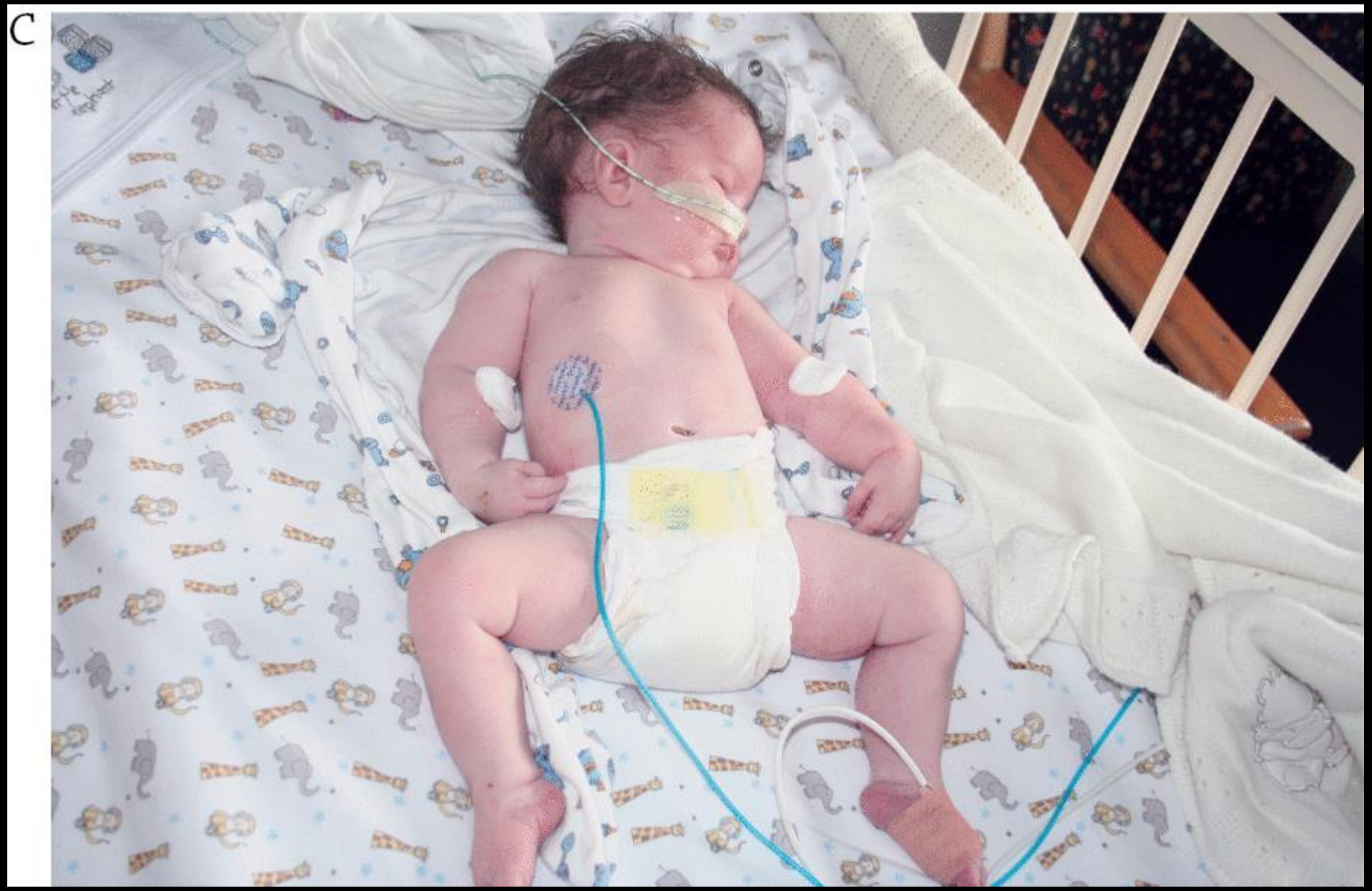
- Decreased fetal movements
- Polyhydramnios
- Oligohydramnios
- Relatively large head to body
- Abnormal hand and foot position

Perinatal

- Increased rate of assisted delivery or C-section
- Increased rate premature and postmature births
- Birth weight typically low or low normal

Neonatal

- Hypotonia
- Poor suck
- Weak cry
- Males: undescended testes, hypoplastic scrotal sac
- Females: hypoplastic labia



https://oxfordmedicine.com/

Floppy babies

1. Safe neonatal care
2. Treat and test for
    1. Infection
    2. Metabolic
    3. Endocrine
3. Consider broad differential diagnosis
4. Follow local protocol for investigations
5. Watch out for dual diagnosis
6. Communicate openly and cautiously

Genetic or acquired?

Transient, stable or progressive?

Originating from:

- *Central nervous system*
- *Spinal cord*
- *Neuromuscular junction*
- *Muscle*

PWS across the lifespan

Infancy

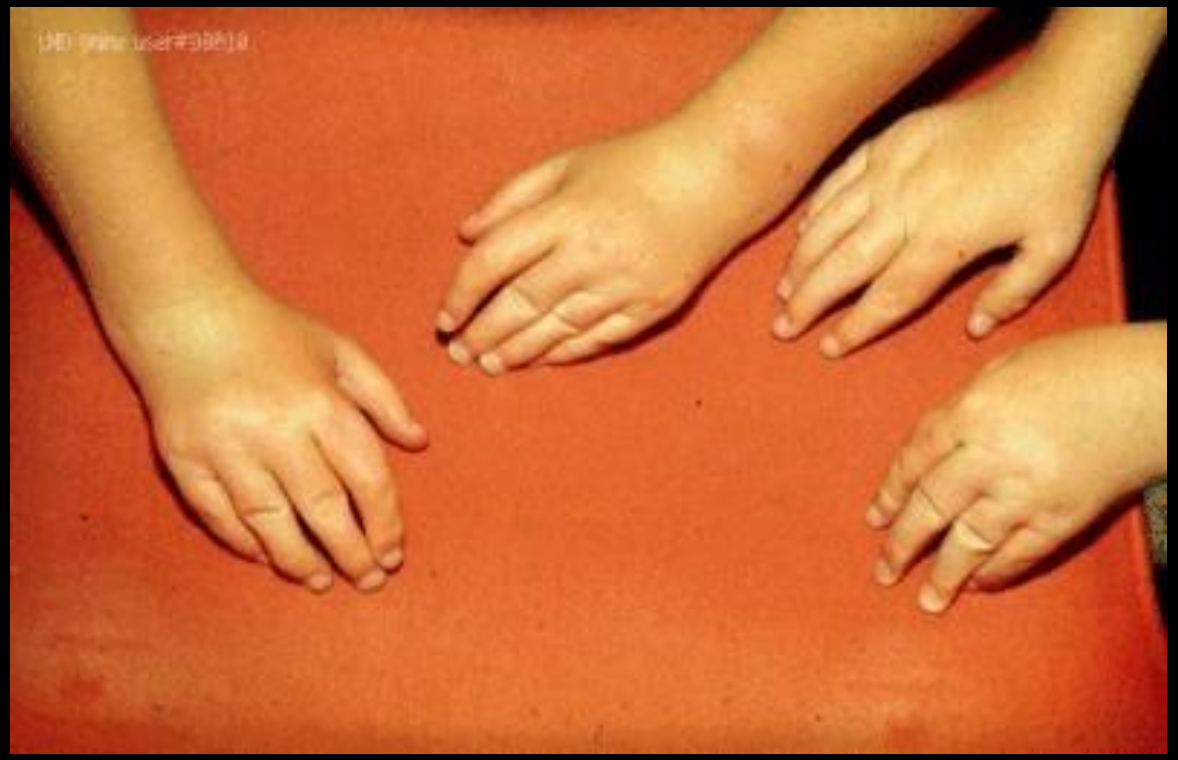
- Feeding difficulties
- GORD
- Poor weight gain
- Hip dysplasia
- Strabismus
- Developmental delay

Early childhood

- Gradual increase in appetite and weight
- Transition to hyperphagia
- Endocrine deficiencies
- Facial and digital features
- Febrile seizures
- Developmental delay

Later childhood

- Obesity
- Sleep problems
- Sleep apnoea and abnormal breathing patterns
- Gastrointestinal dysmotility
- Premature adrenarche
- Learning difficulties
- Skin picking
- Repetitive and restricted behaviours
- Emotional storms



face2gene.com

Overweight child with developmental delay

Social and environmental

- Diet
- Medication
- Physical exercise
- Familial

Endocrine

- Hypothyroidism
- Growth hormone deficiency
- Cushing syndrome

Genetic syndromes

- PWS
- Fragile X Syndrome
- Ciliopathies incl Bardet Biedl Syndrome
- Cohen Syndrome
- Many ultra-rare single gene disorders

Lancet 2010

PWS across the lifespan

Adolescence

- Dietary control
- Secondary consequences of obesity
- Delayed puberty
- Scoliosis
- Intellectual disabilities
- Social interactions and relationships
- Depression and anxiety

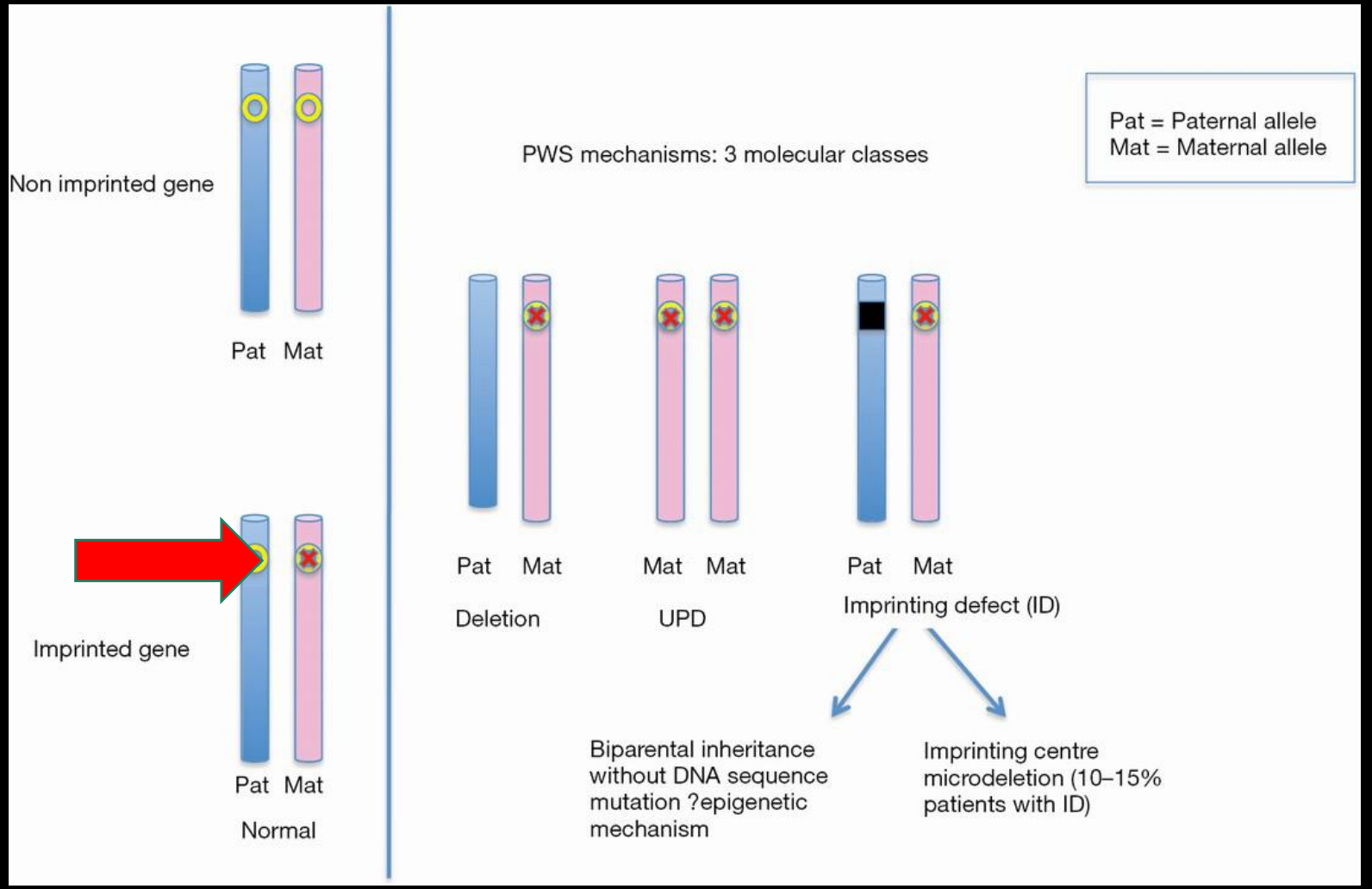
Early adulthood

- Transitions to supported independence and occupation
- Management of diet and physical health
- Minimising secondary health consequences
- Low bone mineral density
- Mental health including psychosis

Later adulthood

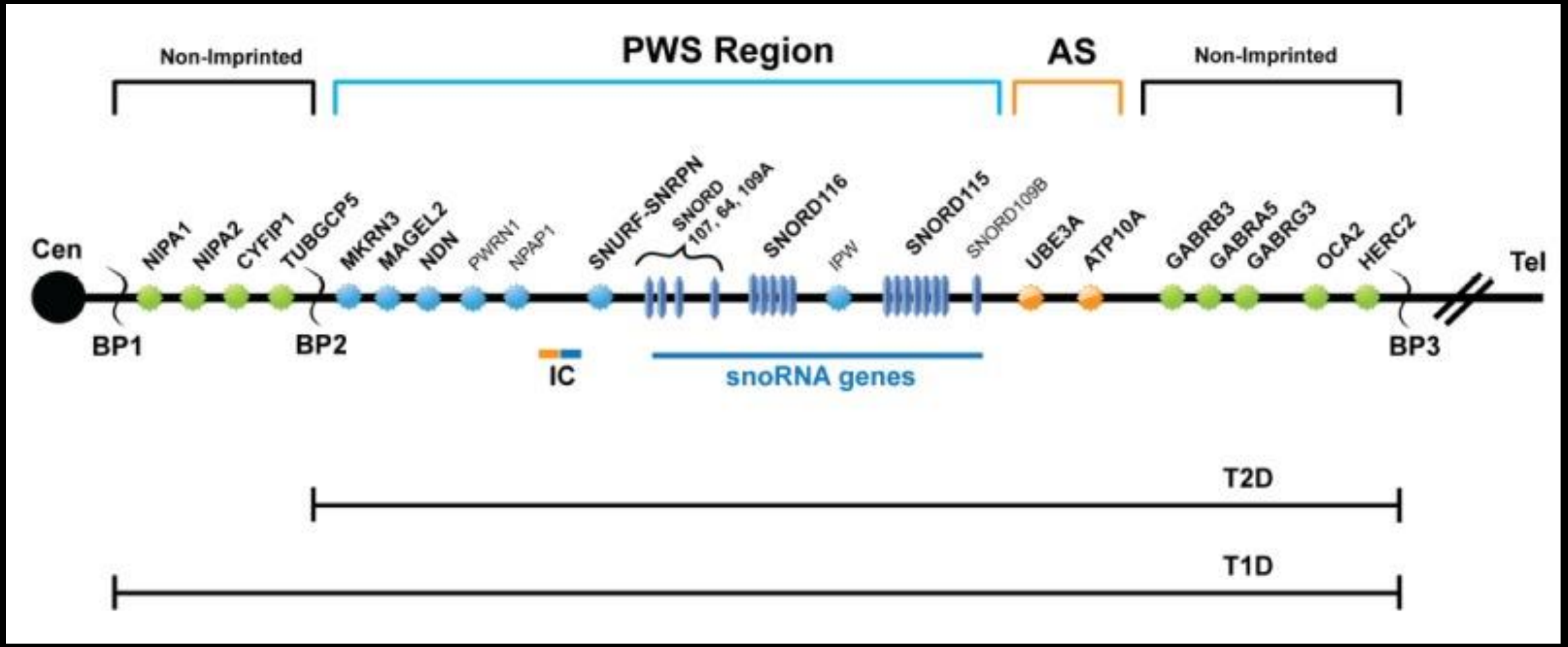
- Ongoing physical and mental health needs

Genetic basis for PWS



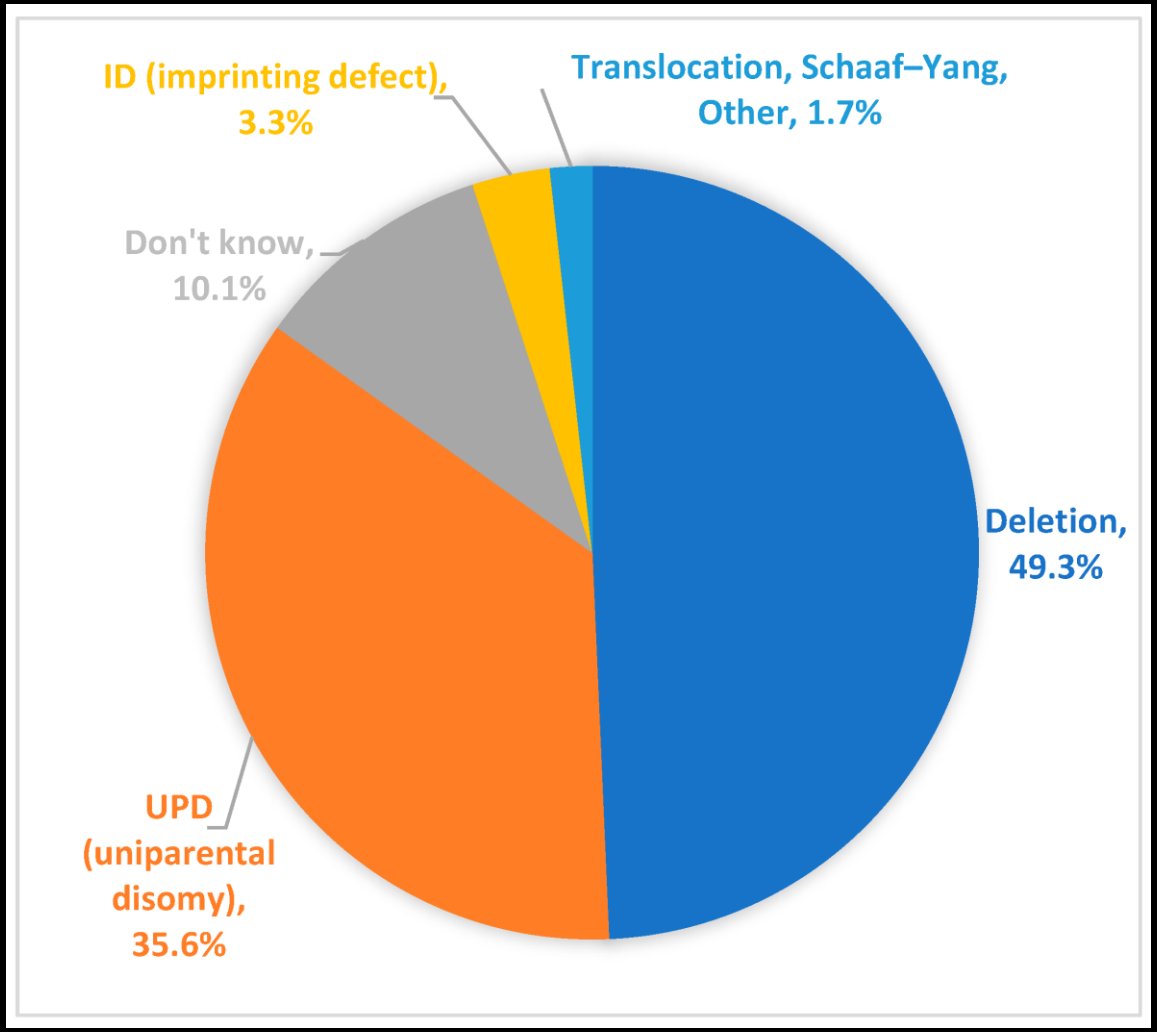
Smith and Hung *Translational Pediatrics* 2017

Genetic basis for PWS



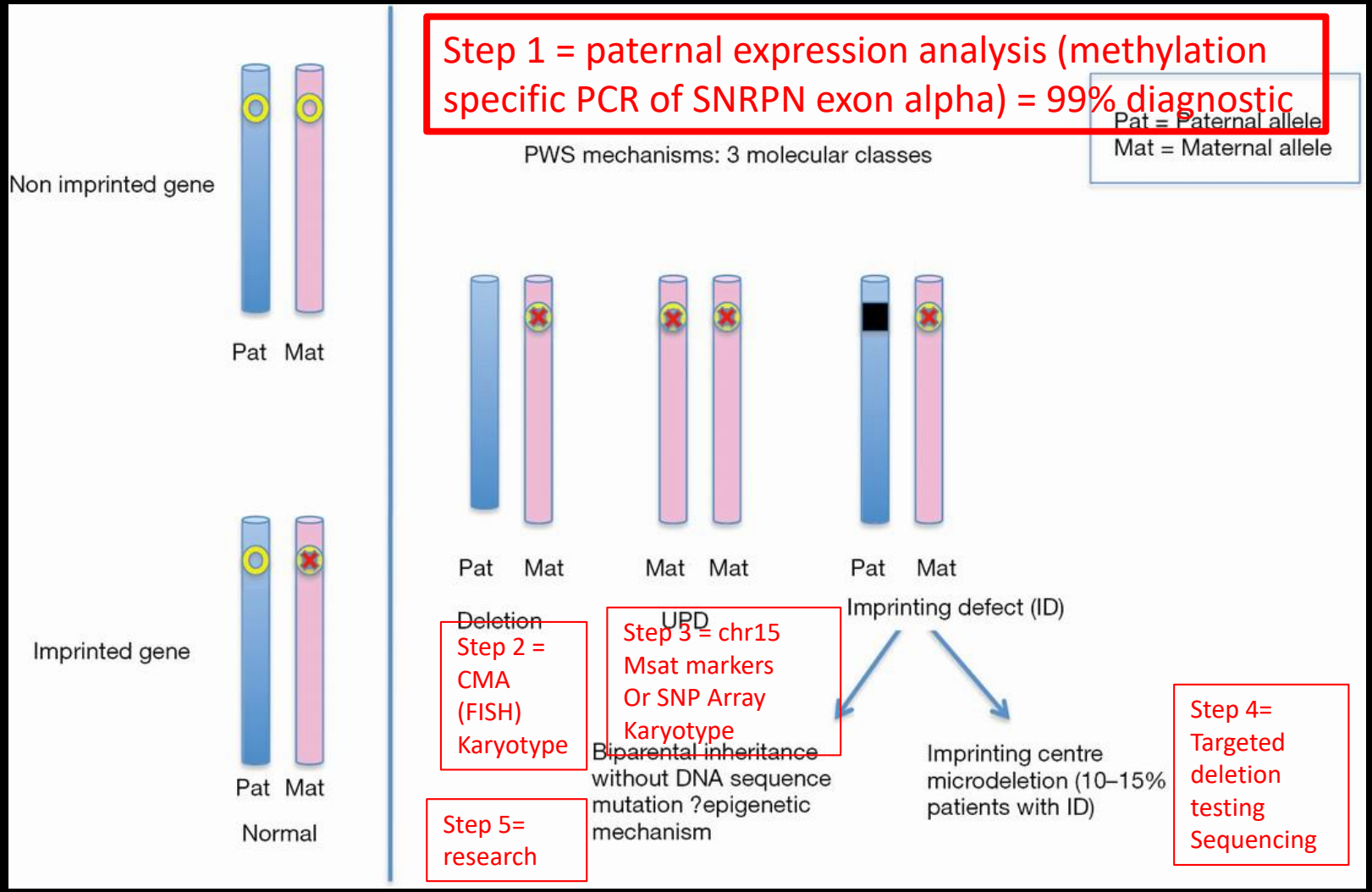
Gene reviews

Genetic basis for PWS



Global Prader–Willi Syndrome Registry. *Genes* (2019)

Genetic testing for PWS



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Summary

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THANK YOU!