

MEDICAL REHABILITATION IN PITT-HOPKINS SYNDROME: CHALLENGES AND CLINICAL PERSPECTIVES- CASE REPORT

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BRIEF HISTORY



1978

PTHS was first described by David Pitt and Ian Hopkins in the Australian Pediatric Journal.



2007

Haploinsufficiency of TCF4 was first shown to be connected to PTHS.



2009

Pitt Hopkins Syndrome Foundation was founded in the Netherlands.



2013

The Pitt Hopkins Research Foundation became its own non-profit organization.



2014

The Pitt Hopkins Syndrome Italian Association was formed.



2016

Pitt Hopkins UK was founded on May 17th.



2019

The Pitt Hopkins Research Foundation announces a clinical trial for microbiota transfer therapy.



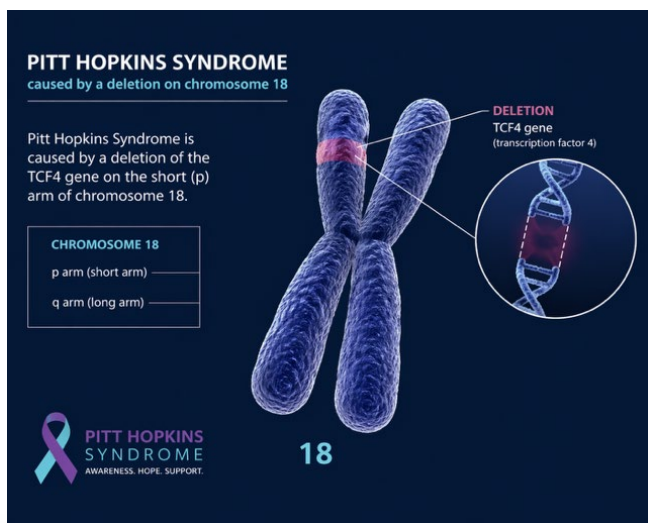
2022

Clinical trials began to study the safety, tolerability, pharmacokinetics, and efficacy of NNZ-2591 in children and adolescents with PTHS.



Definition

Pitt Hopkins Syndrome (PTHS) is a ultra-rare genetic disorder caused by haploinsufficiency of TCF4, that causes developmental delays and varying intellectual disabilities. Patients typically start experiencing symptoms in childhood and delays in reaching certain developmental milestones.



PITT HOPKINS SYNDROME

Common Features and Clinical Characteristics

	DELAYED SITTING	Children with Pitt Hopkins Syndrome typically have a delay in achieving the ability to sit independently.
	DELAYED WALKING	There is a delay in achieving independent walking, often several years later than typical development or not achieved at all in some individuals.
	DISTINCTIVE FACIAL FEATURES	Characteristic facial appearance, including a broad forehead, deep-set eyes, widely spaced eyes, full cheeks, and a pointed chin.
	CROSSED EYES (STRABISMUS)	Misalignment of the eyes is common.
	ATAXIA	Impaired balance and coordination, leading to an unsteady or incoordinated movement pattern.
	HYPERVENTILATION	Episodes of rapid or deep breathing that occur periodically, often without an obvious cause.
	APNEA	Pauses in breathing during sleep are common and can vary in length.
	EASILY AGITATED	Individuals may be easily upset, anxious, or irritable, with a low threshold for frustration.
	OVEREXCITED	Periods of intense excitement or overexcitement can occur, often appearing suddenly and being difficult to calm.



Pitt Hopkins Syndrome is a rare genetic disorder caused by mutations or deletions in the TCF4 gene. Features can vary in severity. Early recognition and supportive interventions can improve quality of life.

Diagnosis

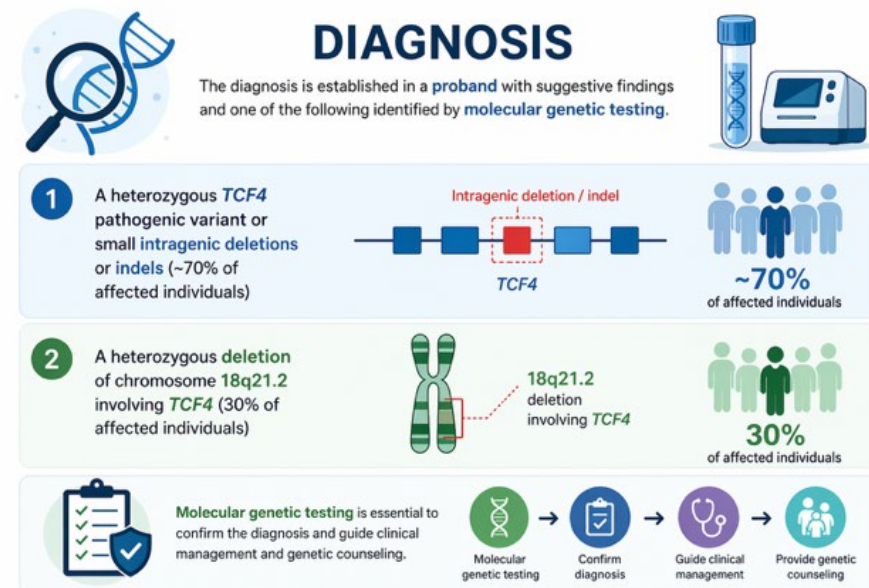
Prevalence? Unknown

Incidence? 1 in

34.000/41.000/225.000

The diagnosis of PTHS is established in a proband with suggestive findings and one of the following identified by molecular genetic testing

- A heterozygous *TCF4* pathogenic variant or small intragenic deletions or indels (~70% of affected individuals)
- A heterozygous deletion of chromosome 18q21.2 involving *TCF4* (30% of affected individuals)



WHY REHABILITATION MATTERS IN THIS CASE

Rationale of the Study

MAJOR CHALLENGES



Severe developmental delay
Affects motor, cognitive, communication and functional skills



Minimal or absent speech
Limits communication and social participation



Motor impairment
Hypotonia, ataxia, poor balance and coordination impact mobility and independence



Breathing abnormalities and epilepsy
Increase medical complexity and vulnerability



Limited access to therapy
Early intervention opportunities are often missed



These challenges result in major limitations in daily activities, participation and quality of life.



HOW REHABILITATION HELPS



Improves motor function
Strength, balance, coordination and gait



Enhances independence
Supports daily activities and self-care



Promotes participation
Facilitates engagement in family, school and community life



Improves quality of life
Reduces caregiver burden and supports well-being



Critical when access is limited
Individualized programs and home exercises can reduce disparities



Rehabilitation remains essential, even when delivered at a lower frequency.



RATIONALE OF THIS STUDY

To highlight the challenges and clinical perspectives of rehabilitation in a pediatric patient with Pitt-Hopkins Syndrome who receives therapy at a restricted frequency due to socioeconomic limitations.



Understanding the impact of limited therapy access is essential to advocate for equitable rehabilitation services and to identify effective strategies that can optimize functional outcomes in rare disorders.

Aim of the study





CASE PRESENTATION

1. PATIENT IDENTIFICATION



Age: 13 years
Sex: Female
Diagnosis: Pitt–Hopkins Syndrome
(TCF4 mutation)

2. CLINICAL PROFILE



Severe motor impairment
 Marked limitations in mobility and
gross motor function



Profound cognitive impairment
 Severe delay in cognitive development
and adaptive functioning



Delay in expressive speech
 Limited verbal communication



Strabismus
 Present



Enuresis
 Urinary incontinence



Hypotonia
 Generalized low muscle tone



PITT–HOPKINS SYNDROME (PTHS)

*A rare neurodevelopmental disorder
characterized by global developmental
impairment and multisystem involvement.*

3. REHABILITATION CONTEXT



Low-frequency rehabilitation
due to financial limitations
and limited access to regular
therapy services.

Frequency: 1 session per week

4. REHABILITATION RECEIVED



Physiotherapy
 To improve motor function, posture
and mobility



Occupational Therapy
 To enhance daily living skills and
independence



Balance Training
 To improve postural control
and stability



Functional Activities
 Task-oriented activities to promote
participation

5. ASSESSMENTS PERFORMED



Ashworth Scale – Spasticity assessment



GMFM–88 – Gross motor function



PEDI – Functional skills and
caregiver assistance



Berg Balance Scale – Balance assessment



PURPOSE OF THIS CASE STUDY

To analyze functional outcomes in a pediatric patient with Pitt–Hopkins Syndrome
and explore the impact of low-frequency rehabilitation (1 session/week) on motor
function, daily activities and participation.



Understand
functional impact



Inform clinical
practice



Advocate for equitable
rehabilitation access



Improve quality of life
and participation

FUNCTIONAL OUTCOMES – ASSESSMENT RESULTS

 **Results after 6 months of rehabilitation (1 session per week)**



1. ASHWORTH MODIFIED SCALE

(Spasticity Assessment)

BODY REGION	SCORE (0–4)	INTERPRETATION
 Upper Limbs	3	Considerable increase in muscle tone
 Lower Limbs	2	More marked increase in muscle tone

SCORE INTERPRETATION

0 = No increase in tone 1 = Slight increase 1+ = Slight increase, catch & release
 2 = More marked increase 3 = Considerable increase 4 = Affected part(s) rigid



2. GMFM-88

(Gross Motor Function Measure)

DIMENSION	RAW SCORE (Obtained)	MAXIMUM SCORE	PERCENTAGE (%)
A. Lying & Rolling	27	51	52.9%
B. Sitting	17	60	28.3%
C. Crawling & Kneeling	2	42	4.8%
D. Standing	6	39	15.4%
E. Walking, Running & Jumping	10	72	13.9%
TOTAL GMFM-88 SCORE	23.1%		

**TOTAL GMFM-88
SCORE**



Overall gross motor function is 23.1% of the maximum possible score.



3. PEDI – FUNCTIONAL SKILLS

(Pediatric Evaluation of Disability Inventory)

DOMAIN	SCORE (0–100)	INTERPRETATION GUIDE
Self-Care	3	Severe difficulty / Very low independence
Mobility	2	Severe difficulty / Very low independence
Social Function	2	Severe difficulty / Very low independence

Higher scores indicate greater functional independence.



4. BERG BALANCE SCALE

(Balance Assessment)

TOTAL SCORE (0–56)	INTERPRETATION GUIDE
8	0–20: High risk of falling 21–40: Medium risk of falling 41–56: Low risk of falling

TOTAL BERG SCORE



Significantly impaired balance and postural control.



Assessments across all four standardized scales indicate severe functional limitations in motor performance, daily activities, and balance, highlighting the need for continued and intensified rehabilitation.



FUNCTIONAL IMPROVEMENTS ACHIEVED with Low-Frequency Rehabilitation (1 session per week)



Despite the limited therapy frequency, meaningful functional gains were observed over 6 months of intervention.

1 STANDING UP BEFORE Unable to stand independently AFTER Able to stand with assistance or support ✓ Better postural control and weight-bearing capacity.	2 BETTER UPPER BODY CONTROL (SITTING & WALKING) BEFORE Poor trunk control; needed maximal support AFTER Improved trunk control in sitting and walking ✓ Improved postural stability and control of the upper body.	3 MORE STABLE GAIT – WIDER STEPS BEFORE Scissors gait, narrow base of support AFTER Wider base of support, more stable steps ✓ Improved balance, gait stability and safety.	4 GRASPS AND HAND FUNCTION BEFORE Unable to grasp objects AFTER Able to grasp objects with hands ✓ Emerging hand function and intentional grasp.	5 PLACING SELF AT THE EDGE OF THE BED (WHEN STIMULATED) BEFORE Unable to move or position herself at the edge AFTER Can move and place herself at the edge of the bed with stimulation ✓ Improved initiation, motor planning and functional mobility.
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These functional gains, achieved with only 1 session per week, highlight the child's potential for progress and the importance of access to regular, intensive rehabilitation.





CONCLUSION & TAKE-HOME MESSAGE

Low-Frequency Rehabilitation in Pitt-Hopkins Syndrome



CONCLUSION



Pitt-Hopkins Syndrome is associated with **severe and complex functional impairment** affecting motor control, balance, and independence.



Even with low-frequency rehabilitation (1 session/week), **measurable functional gains** can be achieved.



Progress remains limited and slower compared to intensive rehabilitation programs.



Functional outcomes are strongly influenced by **therapy intensity, caregiver involvement, and access to services.**



This case highlights **the critical role of rehabilitation** as a long-term management strategy in rare neurodevelopmental disorders.



TAKE-HOME MESSAGE

“

Rehabilitation is effective even at low frequency – but access and intensity determine the real potential for recovery.

”



In rare neurodevelopmental disorders like Pitt-Hopkins Syndrome, **access to rehabilitation is not optional – it is a determinant of functional outcome.**

KEY MESSAGE IN PRACTICE



Even small doses of therapy can lead to real improvements.



Consistency and long-term commitment are essential.



Caregiver involvement maximizes carry-over to daily life.



Greater access and intensity can unlock even greater potential.



**STRONGER ACCESS
BETTER OUTCOMES**

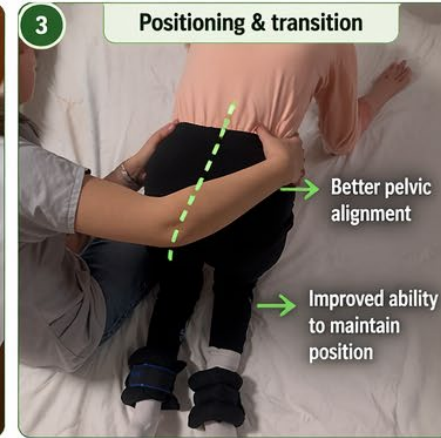


FUNCTIONAL IMPROVEMENTS – CLINICAL OBSERVATION

Results after 6 months of rehabilitation (1 session per week)



1. POSTURAL CONTROL & ASSISTED STANDING



KEY TAKEAWAY

- ✓ Assisted standing achieved
- ✓ Improved trunk stability
- ✓ Initiation of functional positioning
- ✓ Better postural control



2. GAIT STABILITY & EMERGING FUNCTIONAL USE



KEY TAKEAWAY

- ✓ Wider base of support during gait
- ✓ Improved balance and stepping
- ✓ Emerging hand function and task interaction
- ✓ Greater participation in daily activities



These functional changes, although subtle, are clinically meaningful and highlight the positive impact of consistent rehabilitation, even at low frequency.





Thank You!

This case highlights that **meaningful functional gains are possible, even with low-frequency rehabilitation**, in a child with Pitt-Hopkins Syndrome.



REHABILITATION
is not just about movement – it is about **unlocking potential**.



CONSISTENT INTERVENTION
even at low intensity, can lead to **meaningful improvements**.



CAREGIVER INVOLVEMENT
and a supportive environment are **essential** to progress.



EVERY CHILD WITH PTHS
is **unique** – individualized goals make a difference.



OUR HOPE
is that this case inspires greater access to rehabilitation and a **better future** for every child.

“ In this case, progress was **not defined by intensity – but by persistence**. ”



*Small steps today,
brighter tomorrows.*



Thank you for your attention.
Together, we can help every step count.



Collaboration



Compassion



Progress



Hope

