**[DATE]**

Dear Dr. **[NAME]**,

Our child, **[NAME]**, has been diagnosed with a condition called 4H Leukodystrophy (or POLR3-Related Leukodystrophy), where the 4Hs stand for hypomyelination, hypodontia, and hypogonadotropic hypogonadism. This rare, neurodegenerative condition is inherited in an autosomal recessive manner.

Our child has a **[SPECIFIC MUTATION]** in the **[POLR3B/POLR3A/POLR1C/POLR3K]** gene. In our child, we first saw symptoms during **[INFANCY/CHILDHOOD/ADOLESCENCE/ADULTHOOD]** and they were diagnosed at **[AGE]**.

*Please refer to the next page for additional medical resources in caring for Leukodystrophy patients.*

**Common Symptoms/Findings**

Common findings in these patients include stiff limbs and limited fine motor development, dysarthria, learning disabilities, and delayed or atypical puberty, sialorrhea, dysphagia, epilepsy, hip dislocations, ataxia, and gait issues. About half of 4H Leukodystrophy patients have short stature and can have delayed tooth eruption with teeth appearing out of the typical order. Additionally, most 4H children may have an abnormal gait or tremors. All 4HL cases are highly variable and will need customized care. Because of this, not all 4HL patients will exhibit every symptom listed above, but our child, specifically, does have [\_\_\_\_\_, \_\_\_\_\_\_, \_\_\_\_\_\_] symptoms.

“4H is an insidiously progressive disorder with declining motor function due to increasing ataxia, sometimes with episodes of faster deterioration triggered by minor infections. 4H leukodystrophy comes with a spectrum of disease severity. At the milder end of the spectrum, patients present after age 5 years with learning difficulties and motor clumsiness. Exceptionally, patients become symptomatic only in late adolescence or early adulthood. It is likely that this late-onset group represents an underestimation, since clinical presentation of this age group is mild, with one family even diagnosed by chance.” (Wolf et al., 2014).

**Faster decline can occur during times of high stress and illness. A fever should be treated liberally with antibiotics. Please note that most 4HL patients will have difficulty swallowing so a feeding tube may need to be placed while in-patient.**

**Prognosis and Progression**

This condition is severe, but there is a wide variability of clinical severity. Most children will initially have typical physical development for their age (aside from short stature) but will experience progression of the condition over time, especially in terms of gait and motor function. As Dr. Wolf states in her 2014 paper, “At the severe end, affected children do not achieve independent walking and have mild to moderate intellectual disability” (Wolf et al., 2014). In this way, 4HL can have variable severity, but in most, if not all, cases 4HL is progressive and life-limiting.

**Specialists**

Children with this condition are often followed by neurology, pulmonology, odontology, ophthalmology, endocrinology, and other rehabilitation specialists. Our child **[WILL BE/IS]** seen by endocrinology every 4 years for delayed puberty, seen by neurology every 6 months for decreasing white matter, ophthalmology on a regular basis for myopia, pulmonology, or otolaryngologist every \_\_\_\_ **[YEARS/MONTHS]** for issues with swallowing and drooling. Most 4HL children will need a baseline swallowing study with this otolaryngologist and routine follow-up. In addition to the specialists, pelvic x-rays every 2 years are recommended for the common hip displacement with 4HL children. Our child **[WILL BE/IS]** also seeing a team of rehabilitation specialists including speech therapy \_\_\_\_\_ hours a week, occupational therapy for \_\_\_\_ hours a week.

**Treatment**

All treatments currently in practice are supportive for specific patient’s symptoms, but no cures currently exist. Our child has been treated with \_\_\_\_\_ previously for \_\_\_\_\_\_.

*Listed below are other supportive treatments for specific 4HL symptoms.*

Artane (or anticholinergic medication trihexyphenidyl) has proven useful in treating generalized dystonia for 4HL patients. L-Dopa has also been used as a treatment for some 4H Leukodystrophy patients since it is a more advanced measure in treating generalized dystonia. While anti-convulsant medications are helpful for the 4HL children with seizures, some may have detrimental effects on bone health. Commonly, G-tubes or J-tubes can be used to combat malnutrition from the difficulty swallowing in combination with speech and physical therapy. These children should be checked periodically with bone density scans for this reason. (Adang et al., 2017)

Other up-to-date literature on treatments can be found on the Yaya Foundation website Research library.

**References for your Practice**

OMIM.org:

[*POLR3A, #607694*](https://omim.org/entry/607694?search=leukodystrophy&highlight=leukodystrophy)

[*POLR3B, #614381*](https://omim.org/entry/614381?search=polr3b&highlight=polr3b)

[*POLR1C, #616494*](https://omim.org/entry/616494?search=polr1c&highlight=polr1c)

[*POLR3K, #619310*](https://omim.org/entry/619310?search=polr3k&highlight=polr3k)

Yaya Foundation for 4H Leukodystrophy Research library:

<https://yayafoundation4hl.org/research-articles/>

**Resources for your Patients**

Yaya Foundation for 4H Leukodystrophy:

<https://yayafoundation4hl.org/>

Facebook Groups (POLR3 Caretakers/4H Leukodystrophy):

<https://www.facebook.com/groups/4hsyndrome>

Living with Leukodystrophy eBook (free):

<https://www.curemld.com/product-page/living-with-leukodystrophy-ebook>