Chapter 8
Print ISBN: 978-93-49970-37-3, eBook ISBN: 978-93-49970-88-5

Allan-Herndon-Dudley-Syndrome: An Overview of an Extremely Rare Disorder in Childhood

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DOI: https://doi.org/10.9734/bpi/nhstc/v2/5685

Peer-Review History:
This chapter was reviewed by following the Advanced Open Peer Review policy. This chapter was thoroughly checked to prevent plagiarism. As per editorial policy, a minimum of two peer-reviewers reviewed the manuscript. After review and revision of the manuscript, the Book Editor approved the manuscript for final publication. Peer review comments, comments of the editor(s), etc. are available here: https://peerreviewarchive.com/review-history/5685

ABSTRACT

Allan-Herndon-Dudley syndrome (AHDS) is a rare X-linked disease with severe neuropsychiatric abnormalities including psychomotor retardation, lack of speech development, dystonia, and severe intellectual deficits. William Allan, Florence C. Dudley, and C. Nash Herndon first described a syndrome which results from the disturbed formation of two thyroid hormone transporters, MCT8 and Oatp1c1. Nearly 320 individuals of around 130 families have been described so far with MCT-8 deficiency. The first individual treatment attempt with LT4 and Propylthiouracil was introduced in 2008; the development of therapies for Allan-Herndon-Dudley syndrome has gained momentum in recent years. Treatment options range from symptomatic interventions, including botulinum toxin injections, levodopa/carbidopa, assistive devices, functional therapies, rehabilitation to replacement therapies (LT3, LT4, DIPTA, TRIAC, TETRAC), and gene therapy. Diagnosis, treatment and cure of Allan-Herndon-Dudley syndrome in childhood remains challenging for the future. Due to the low number of cases, conducting large-scale studies is challenging, and therefore, it is difficult to find clear guidelines for this extremely rare disease in childhood.

Keywords: MCT8; child; thyroid transporter-analogon; treatment; genetics.

1. INTRODUCTION

Allan-Herndon-Dudley syndrome (AHDS), also known as MCT8 (monocarboxylate transporter 8) deficiency, is a rare genetic disorder resulting from a defect in the

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transport of thyroid hormone into the central nervous system (CNS) due to a lack of thyroid hormone transporter protein, MCT8 (Khan et al., 2024, Park et al., 2024). “First described in 1944 by William Allan, Florence C. Dudley, and C. Nash Herndon, where they described a misfunction of two thyroid hormone transporters” (Allan et al., 1994, Ramon-Gomez et al., 2024). AHDS is a severe form of psychomotor retardation characterized by abnormal serum TH values and symptoms of peripheral thyrotoxicosis (Mayerl et al., 2022, Reinwald et al., 2022). “More than 100 families and more than 300 individuals were described in the literature to date” (Allan et al., 1944, Groeneweg et al., 2020, Frints et al., 2008, Sriram et al., 2024). “There is an unknown incidence of involved cases to date due to the small population (Groeneweg et al., 2020). Males are primarily included; only a few female cases have been described so far” (Frints et al., 2008, Sriram et al., 2024, Chakraborty and Das, 2025, Olivati et al., 2022, Beheshti et al., 2022). The disease includes symptoms like congenital hypotonia, most often found at birth or in the first weeks after delivery, which shows progressive states to spasticity with contractures. Babinski's sign is detected early in life. Hyperreflexia will be found later in life (Allan et al., 1944, Groeneweg et al., 2020, Frints et al., 2008, Sriram et al., 2024, Boccone et al., 2020, Yiu et al., 2023). Affected male patients exhibit muscle hypoplasia and muscle weakness in early childhood, resulting in disturbances of head control and motor milestones, which are found to be delayed (Groeneweg et al., 2020, Bittmann, 2024). In nearly all patients, hypotonia and severe intellectual deficits are found (Groeneweg et al., 2020). “Psychomotor disturbances are found from delivery, a delay in motor and speech milestones and autonomous function is never achieved.

The facial impression has characteristic features that start and ameliorate over time: open mouth situation, tense upper lip, ptosis of the left or right eye, abnormal ear folding, thickening of soft tissues of the nose and ears, and deformed or rotated earlobes” (Groeneweg et al., 2020, Remerand et al., 2019). “Long, thin, everted feet are also typically found in many patients. Rotatory nystagmus and disconjugate eye movements are rare features in the eyes. Some patients can develop seizures and poor weight gain with low weight percentiles (Bittmann, 2024). Pectus excavatum and scoliosis manifestations are also infrequently present, as a result of hypotonia and muscle hypoplasia. AHDS is induced most often by mutations in the SLC16A2 gene (Xq13.2), which encodes the monocarboxylate transporter 8 (MCT8), a transporter for thyroid hormone T3. The causative mutations show chain terminations, deletions preserving the reading frame, as well as nonsense and missense mutations (Bittmann, 2024). Neurological problems occur due to the functional loss of transport of the thyroid hormone T3 into special neuronal cells.

Clinical findings reveal the diagnosis and normal and altered thyroid hormone found in serum: male patients have high 3,3',5'-triiodothyronine (T3) levels, low to normal free tetraiodothyronine (T4) levels, and normal to mildly elevated TSH levels, but sometimes low TSH, which is found to be unexpected” (Boccone et al., 2010). “A few countries focus on inclusion in the newborn screening” (Yiu et al., 2023). “A molecular analysis shows mutations in the SLC16A2 gene, and this confirms the diagnosis of AHDS” (Groeneweg et al., 2020). Differential diagnoses focus on diseases with X-linked intellectual disability associated with ataxia,

spastic paraplegia, muscle hypoplasia, X-linked intellectual disability with spastic paraplegia and iron deposition, X- linked progressive cerebellar ataxia and spastic paraplegia type 2 (Bittmann, 2024).

Snyder-Robinson syndrome or Pelizaeus-Merzbacher disease should also be focused on (Inoue, 2019, Osório and Goldman, 2018, Schwartz et al., 2013, Starks et al., 2018). Prenatal diagnosis is thinkable in families if a disease-causing mutation has been clearly ruled out. The way of transmission is X-linked recessive. Genetic counselling should be offered to affected families to identify carriers of an SLC16A2 mutation. Currently, there is no treatment for the disease; only supportive therapy is helpful, but not curative (Bittmann, 2024). Physiotherapy, occupational therapy, and language therapy can be helpful in any way. Dystonic episodes can be treated with different medications, anticholinergics, L-DOPA, carbamazepine, and baclofen therapy. Antiepileptic drugs can help control seizures (Bittmann, 2024). Treatment of hypothyroidism is not helpful. Concerning survival, some patients have survived into their 60s. The overall life expectancy is delayed, and quality of life is restricted. Most patients are unable to sit, stand, or walk independently.

2. EMPIRICAL REVIEW

The rare syndrome, first described in 1944 by William Allan, Florence C. Dudley, and C. Nash Herndon, shows an impaired formation of two thyroid hormone transporters (Allan et al., 1944). The result is the inability of nerve cells, which rely on thyroid hormones, to take up these important hormones into cells (Bittmann, 2024). Allan-Herndon-Dudley syndrome is characterised in male patients and to date only a few females by neurological symptoms with hypotonia and feeding problems in the newborn period, developmental disturbances and intellectual delay ranging from mild to profound and late-onset or occurring pyramidal signs (Frints et al., 2008, Sriram et al., 2024, Quesada-Espinosa et al., 2021). Extrapyramidal symptoms like dystonic movements, choreoathetotic movements, paroxysmal movement disorder, hypokinesial states, masked facial impressions and seizures, often with drug resistance, were present (Bittmann, 2024). Approximately 320 patients with a pathological variant in SLC16A2 have been described in the published world literature (Allan et al., 1944, Groeneweg et al., 2020).

Additional symptoms can include dysthyroidism, showing as poor weight gain, low muscle mass, and varying cold intolerance, sweating, tachycardia, irritability and pathognomonic thyroid tests (Bittmann, 2024). Many female heterozygous patients are not clinically ill but can have minimal thyroid test abnormal results (Frints et al., 2008, Sriram et al., 2024). AHDS can be found most commonly in male patients but also in a few cases in females, as stated above (Frints et al., 2008, Sriram et al., 2024). One female teenager showed the typical features of AHDS and primary ovarian insufficiency in a case report description (Sriramet al., 2024). In another case report, frameshift variants were described (Starks et al., 2018). A 2-year-old Japanese child was diagnosed with MCT8 deficiency according to a new frameshift variant, identified as NM_006517.5(SLC16A2_v001): c.966dup

[p.(Ile323Hisfs*57)] variant (Starks et al., 2018). (Bittmann, 2024). The child, a male patient, showed serious developmental disturbances, with no head muscular control and inability to speak words with a clear meaning (Wakabayashi et al., 2021). Missense or in-frame mutations of SLC16A2 result normally in milder symptoms and late-onset pyramidal signs; loss-of-function mutations are described to have more severe clinical manifestations (Wakabayashi et al., 2021). Variants which include an intracellular C-terminal tail of MCT8 were described as not harmful unless they found frameshifts that lengthen the MCT8 protein significantly (Wakabayashi et al., 2021). This information seems to give clinical advice on evaluating the significance and importance of variants in the C-terminal domain of MCT8 (Geest et al., 2021, Bittmann, 2024). MCT8 deficiency includes severe locomotor and psychomotor disturbances due to inadequate TH transport across the molecular brain barrier and interfered neural TH action (Anık et al., 2014). In a mice study, Mct8/Oatp1c1 double knockout (DKO) mice served as an animal model for MCT8 deficiency, showing in detail central TH deprivation, locomotor delay, and similar histomorphological features as MCT8 patients (Siemes et al., 2023). The mechanisms behind these neurological and motoric symptoms are not ruled out and are not clearly understood in detail (Bittmann, 2024). In the aforementioned study, a special proteome analysis of different brain sections from 21-day-old WT and DKO mice was performed, with identification of over 2900 different proteins with the technique of liquid chromatography mass spectrometry (Siemes et al., 2023).

67 of 2900 proteins revealed significant differences between the individual genotypes (Siemes et al., 2023). When comparing the proteomic and RNA-sequencing analysis data, a significant overlap in alterations was detected (Siemes et al., 2023). Consistent with previous scientific results, DKO mice showed reduced myelin-associated protein expression and differences in levels of established neuronal TH-regulated targets (Siemes et al., 2023, Bittmann, 2024). A decreased protein and mRNA expression of Pde10a, an enzyme found in the striatum, crucial for dopamine receptor signalling, in DKO mice, was present (Siemes et al., 2023).

Changes in PDE10A activities are related to dystonic problems, supposing that reduced basal ganglia PDE10A expression may be an important key pathogenic pathway in human MCT8 deficiency (Siemes et al., 2023).

Normal CNS myelination depends on the timely availability of thyroid hormone (TH) to support the differentiation of oligodendrocyte precursor cells (OPCs) into mature cells, the group of myelinating oligodendrocytes (Mayerl and Heuer, 2023). Allan-Herndon-Dudley syndrome, induced by mutations in the TH transporter MCT8, often presents with abnormal myelination (Mayerl and Heuer, 2023, Lee et al., 2017, Azzolini et al., 2014). An important study including the Mct8/Oatp1c1 double knockout (Dko) mouse model, which mimics MCT8 deficiency in human beings and has lower TH transportation across molecular brain barriers, shows persistence of hypomyelination as an important CNS feature (Mayerl and Heuer, 2023, Bittmann, 2024).

The collaborators investigated whether the decreased myelin content in Dko mice is due to impaired oligodendrocyte maturation (Mayerl and Heuer, 2023) “OPC and

oligodendrocyte populations were classified in Dko mice, wild-type mice, and single TH transporter knockout mice at different developmental phases (postnatal days P12, P30, and P120) using multi-marker immunostaining and confocal microscopy" (Mayerl and Heuer, 2023). "Only in Dko mice researchers found a decrease in cells expressing the oligodendroglia marker Olig2, spanning all stages from OPCs to mature oligodendrocytes" (Mayerl and Heuer, 2023). "Dko mice showed an elevated population of OPCs and a lower number of mature oligodendrocytes in both white and grey matter areas at all time points, resuming a blockage in differentiation in the absence of Mct8/Oatp1c1" (Mayerl and Heuer, 2023, Bittmann, 2024).

Cortical oligodendrocyte structural parameters, by quantifying the number of mature myelin sheaths per oligodendrocyte, were analysed. A decrease in myelin sheaths, which were longer in length, was only present in Dko mice, suggesting a compensatory response to the reduced number of mature oligodendrocytes (Mayerl and Heuer, 2023). (Bittmann, 2024). These mechanisms revealed a relation between abnormal myelination state and compromised neuronal function in Mct8/Oatp1c1 deficient animals (Mayerl and Heuer, 2023).

3. DESCRIPTIVE REVIEW

A multidisciplinary team approach should give standard care information for hypotonia, poor feeding, developmental delay/intellectual disability, spasticity, and extrapyramidal movement disorders.

Anticonvulsive medication should be administered by a qualified neurologic paediatrician. Thyroid hormone replacement therapy during childhood is not recommended in AHDS to date, as it may worsen a situation of dysthyroidism (Bittmann, 2024). Children should be checked clinically every six months until the age of four years, then annually for developmental progress or delay, educational support, neurologic disturbances, spine and hip joint analysis, and mobility/self-help skills. Limited therapeutic medications and skills are currently available for treating the disease, with the main focus being on ameliorating the thyrotoxic situation rather than neurological symptoms (Bittmann, 2024). Research focuses on thyroid hormone analogues like TRIAC (Ramon-Gomez et al., 2024, Refetoff et al., 2021), DITPA, and TETRAC (Visser, 2021, Groeneweg et al., 2021, Visser, 2013, Kinne et al., 2010, De Vrieze et al., 2014), which can potentially ameliorate normal organ function without the need for MCT8. Other therapeutic approaches, such as gene replacement therapy and pharmacological chaperones, are also being researched to ameliorate the transport of thyroid hormones through MCT8. Two types of treatment have been studied in MCT8 deficiency. The first involves normalising serum T4 and T3 levels using a "block-and-replace" approach with Propylthiouracile and T4 hormone (Cooper et al., 1983). Treatment of older AHDS patients did not show significant neurological improvement but did have positive effects on body weight, heart rate, and certain blood markers (Bittmann, 2024). These changes are attributed to reduced exposure of peripheral tissues to high serum T3 levels. It is possible that neurological benefits may only be seen if this treatment is started soon after birth. Another potential treatment option is the use

of a *thyroid hormone analogue* that can enter the brain independently of MCT8 (Visser, 2021, Groeneweg et al., 2020, Visser, 2013). Following promising results in MCT8 KO mice with diiodothyropropionic acid (DITPA), a clinical trial was conducted with this analogue in four younger AHDS patients. While this treatment normalised serum T4 and T3 levels and had positive effects on peripheral tissues, including weight gain and heart rate reduction, there was no significant neurological improvement. DITPA has low affinity for T3 receptors, so the thyroid hormone metabolite TRIAC may be a better option for MCT8 patients (Bittmann, 2024). TRIAC has several advantages, including high affinity for T3 receptors, independent cellular uptake, metabolism by DIO3, proven activity in brain cells, availability, and clinical experience in other conditions (Visser, 2021, Groeneweg et al., 2020, Visser, 2013, Bauer, 2019). A multicenter trial is currently investigating the potential benefits of TRIAC treatment in MCT8 patients. Recent studies suggest that treatment with the TRIAC precursor TETRAC may also be beneficial for MCT8 patients (Kinne et al., 2010, De Vrieze et al., 2014). TETRAC allows for the regulation of brain TRIAC levels through DIO2-mediated production (Kinne et al., 2010, De Vrieze et al., 2014). However, there is less clinical experience with TETRAC, and it is not readily available (Kinne et al., 2010, De Vrieze et al., 2014).

4. CONCLUSIONS

The treatment options for MCT8 deficiency or AHDS focus on analysing the specific symptoms present in each individual. Prenatal treatment approaches were performed (Adams et al., 2022). A multidisciplinary team approach of specialists, including pediatric neurologists, pediatric surgeons, pediatric orthopaedists, language pathologists, physical therapists, and other healthcare professionals, may collaborate to elaborate and implement a comprehensive treatment approach for affected individuals (Bittmann, 2024). Clinical trials and studies focus on potential treatments for MCT8 deficiency. The combination of propylthiouracil (PTU) and L-thyroxine (L-T4) has been shown to improve nutritional status. Other treatments being investigated include thyroid hormone analogues, phenylbutyrate (De Vrieze et al., 2014) and gene therapy approaches, though these are still in the experimental stages and childhood shoes and not yet available for widespread use to date (Bittmann, 2024). Early diagnosis and the development of an effective treatment plan will be crucial in addressing the severe symptoms seen in affected individuals. An association with ganglioglioma, intermittent esotropia in 4 siblings and sensorineural hearing loss were described (Quesada-Espinosa et al., 2021, Bauer, 2019, Lee et al., 2017).

Concerning genetic counselling aspects, AHDS is inherited in an X-linked way. If the mother of a proband has a pathogenic variant in the SLC16A2 gene, there is a 50% chance of transmitting it in each pregnancy. Males who inherit the variant will be affected, while females who inherit it will be carriers and typically not show clinical symptoms, though they may have minor thyroid test abnormalities (Bittmann, 2024). Once the pathogenic variant in SLC16A2 has been identified in a family member, carrier testing for at-risk female relatives, prenatal testing for pregnancies at increased risk, and preimplantation genetic testing are options.

A description of characteristics of MCT8 deficiency in a large Dutch patient cohort revealed poor survival with a high prevalence of treatable underlying risk factors, and provides knowledge that might inform clinical management and future evaluation of therapies (Groeneweg et al., 2020). In conclusion, Allan-Herndon-Dudley syndrome is a very rare disease in childhood, and there are only a few effective treatment options (Bittmann, 2024). Like in many other genetic rare diseases, a one-time gene therapy approach would be desirable to cure the disease, but this is, to date, in childhood shoes. Due to the low population, bigger studies are difficult to establish to find clear guidelines for this extremely rare disease in childhood.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that no generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

Adams, J. W., Malicki, D., Levy, M., & Crawford, J. R. (2022). Ganglioglioma with novel molecular features presenting in a child with Allan-Herndon-Dudley syndrome. *BMJ Case Reports, 15*(3), e248734. https://doi.org/10.1136/bcr-2021-248734
PMID: 35236707; PMCID: PMC8895953

Allan, W., Herndon, C. N., & Dudley, F. C. (1944). Some examples of the inheritance of mental deficiency: Apparently sex-linked idiocy and microcephaly. *American Journal of Mental Deficiency, 48*, 325–334.

Anık, A., Kersseboom, S., Demir, K., Catlı, G., Yiş, U., Böber, E., et al. (2014). Psychomotor retardation caused by a defective thyroid hormone transporter: Report of two families with different MCT8 mutations. *Hormone Research in Paediatrics, 82*(4), 261–271.
https://doi.org/10.1159/000365191

Azzolini, S., Nosadini, M., Balzarin, M., Sartori, S., Suppiej, A., Mardari, R., Greggio, N. A., & Toldo, I. (2014). Delayed myelination is not a constant feature of Allan-Herndon-Dudley syndrome: Report of a new case and review of the literature. *Brain and Development, 36*(8), 716–720. https://doi.org/10.1016/j.braindev.2013.10.009
Epub 2013 Nov 19. PMID: 24268987

Bauer, A. J. (2019). Triac in the treatment of Allan-Herndon-Dudley syndrome. *Lancet Diabetes & Endocrinology, 7*(9), 661–663. https://doi.org/10.1016/S2213-8587(19)30217-7
PMID: 31377264

Bauer, A. J. (2019). Triac in the treatment of Allan-Herndon-Dudley syndrome. *Lancet Diabetes & Endocrinology, 7*(9), 661–663. https://doi.org/10.1016/S2213-8587(19)30217-7
Epub 2019 Jul 31. PMID: 31377264

Beheshti, R., Aprile, J., & Lee, C. (2022). Allan-Herndon-Dudley syndrome: A novel pathogenic variant of the *SLC16A2* gene. *Cureus, 14*(1), e21771. https://doi.org/10.7759/cureus.21771
PMID: 35251841; PMCID: PMC8890594

Bittmann, S. (2024). Allan-Herndon-Dudley-Syndrome in Childhood: Is there No Cure? *Asian Journal of Pediatric Research, 14*(7), 79–85.

Boccone, L., Mariotti, S., Dessì, V., Pruna, D., Meloni, A., & Loudianos, G. (2010). Allan-Herndon-Dudley syndrome (AHDS) caused by a novel *SLC16A2* gene mutation showing severe neurologic features and unexpectedly low TRH-stimulated serum TSH. *European Journal of Medical Genetics, 53*(6), 392–395. https://doi.org/10.1016/j.ejmg.2010.08.001

Chakraborty, S., & Das, D. (2025). Allan-Herndon-Dudley syndrome. *Indian Journal of Pediatrics, 92*(6), 635–636. https://doi.org/10.1007/s12098-025-05507-9
Epub 2025 Mar 25. PMID: 40131620

Cooper, D. S., Kieffer, J. D., Halpern, R., Saxe, V., Mover, H., Maloof, F., & Ridgway, E. C. (1983). Propylthiouracil (PTU) pharmacology in the rat. II. Effects of PTU on thyroid function. *Endocrinology, 113*(3), 921–928. https://doi.org/10.1210/endo-113-3-921

de Vrieze, E., van de Wiel, S. M., Zethof, J., Flik, G., Klaren, P. H., & Arjona, F. J. (2014). Knockdown of monocarboxylate transporter 8 (*mct8*) disturbs brain development and locomotion in *Danio rerio*. *Endocrinology, 155*(6), 2320–2330.
https://doi.org/10.1210/en.2013-1962

Frints, S. G., Lenzner, S., Bauters, M., Jensen, L. R., Van Esch, H., des Portes, V., et al. (2008). MCT8 mutation analysis and identification of the first female with Allan-Herndon-Dudley syndrome due to loss of MCT8 expression. *European Journal of Human Genetics, 16*(9), 1029–1037.
https://doi.org/10.1038/ejhg.2008.66

Gagliardi, L., Nataren, N., Feng, J., Schreiber, A. W., Hahn, C. N., Conwell, L. S., Coman, D., & Scott, H. S. (2015). Allan-Herndon-Dudley syndrome with unusual profound sensorineural hearing loss. *American Journal of Medical Genetics Part A, 167A*(8), 1872–1876.
https://doi.org/10.1002/ajmg.a.37075

Groeneweg, S., van Geest, F. S., Abacı, A., Alcantud, A., Ambegaonkar, G. P., Armour, C. M., et al. (2020). Disease characteristics of MCT8 deficiency: An international, retrospective, multicentre cohort study. *The Lancet Diabetes & Endocrinology, 8*(7), 594–605.
https://doi.org/10.1016/S2213-8587(20)30153-4

Groeneweg, S., van Geest, F. S., Peeters, R. P., Heuer, H., & Visser, W. E. (2020). Thyroid hormone transporters. *Endocrine Reviews, 41*(2), bnz008.

Inoue, K. (2019). Pelizaeus-Merzbacher disease: Molecular and cellular pathologies and associated phenotypes. In *Advances in Experimental Medicine and Biology, 1190*, 201–216. https://doi.org/10.1007/978-981-32-9636-7_13

Khan, W. N., Heng, R., & Tobias, J. D. (2024). Perioperative care of a child with Allan-Herndon-Dudley syndrome. *International Journal of Clinical Pediatrics, 13*(2), 48–53.

Kinne, A., Kleinau, G., Hoefig, C. S., Grüters, A., Köhrle, J., Krause, G., & Schweizer, U. (2010). Essential molecular determinants for thyroid hormone transport and first structural implications for monocarboxylate transporter 8. *Journal of Biological Chemistry, 285*(36), 28054–28063. https://doi.org/10.1074/jbc.M110.129577

Lee, J. Y., Kim, M. J., Deliyanti, D., Azari, M. F., Rossello, F., Costin, A., Ramm, G., Stanley, E. G., Elefanty, A. G., Wilkinson-Berka, J. L., & Petratos, S. (2017). Overcoming monocarboxylate transporter 8 (*mct8*)-deficiency to promote human oligodendrocyte differentiation and myelination. *EBioMedicine, 25*, 122–135. https://doi.org/10.1016/j.ebiom.2017.10.016 PMID: 29111262; PMCID: PMC5704066

Mayerl, S., & Heuer, H. (2023). Thyroid hormone transporter Mct8/Oatp1c1 deficiency compromises proper oligodendrocyte maturation in the mouse CNS. *Neurobiology of Disease, 184*, 106195. https://doi.org/10.1016/j.nbd.2023.106195

Mayerl, S., Alcaide Martin, A., Bauer, R., Schwaninger, M., Heuer, H., & Ffrench-Constant, C. (2022). Distinct actions of the thyroid hormone transporters *Mct8* and *Oatp1c1* in murine adult hippocampal neurogenesis. *Cells, 11*(3), 524.

Olivati, C., Favilla, B. P., Freitas, E. L., Santos, B., Melaragno, M. I., Meloni, V. A., & Piazzon, F. (2022). Allan-Herndon-Dudley syndrome in a female patient and related mechanisms. *Molecular Genetics and Metabolism Reports, 31*, 100879. https://doi.org/10.1016/j.ymgmr.2022.100879 PMID: 35782622; PMCID: PMC9248228

Osório, M. J., & Goldman, S. A. (2018). Neurogenetics of Pelizaeus-Merzbacher disease. In *Handbook of Clinical Neurology, 148*, 701–722. https://doi.org/10.1016/B978-0-444-64076-5.00045-4

Park, S., Shin, Y. L., Seo, G. H., & Hong, Y. H. (2024). Late-onset drug resistant epilepsy in an adolescent with Allan-Herndon-Dudley syndrome. *Journal of Genetic Medicine, 21*(1), 31–35.

Quesada-Espinosa, J. F., Garzón-Lorenzo, L., Lezana-Rosales, J. M., Gómez-Rodríguez, M. J., Sánchez-Calvin, M. T., Palma-Milla, C., et al. (2021). First female with Allan-Herndon-Dudley syndrome and partial deletion of X-inactivation center. *Neurogenetics, 22*(4), 343–346. https://doi.org/10.1007/s10048-021-00660-7

Ramon-Gomez, J. L., Cortés-Rojas, M. C., Polania-Puentes, M. J., & Guerrero-Ruiz, G. D. P. (2024). Movement disorder perspectives on monocarboxylate 8 deficiency: A case series of 3 Colombian patients with Allan-Herndon-Dudley syndrome. *Movement Disorders Clinical Practice, 11*(5), 567–570. https://doi.org/10.1002/mdc3.14009

Refetoff, S., Pappa, T., Williams, M. K., Matheus, M. G., Liao, X. H., Hansen, K., Nicol, L., Pierce, M., Blasco, P. A., Wiebers Jensen, M., Bernal, J., Weiss, R. E., Dumitrescu, A. M., & LaFranchi, S. (2021). Prenatal treatment of thyroid hormone cell membrane transport defect caused by *MCT8* gene mutation. *Thyroid, 31*(5), 713–720. https://doi.org/10.1089/thy.2020.0306 PMID: 32746752; PMCID: PMC8110025

Reinwald, J. R., Weber-Fahr, W., Cosa-Linan, A., Becker, R., Sack, M., Falfan-Melgoza, C., ... & Sartorius, A. (2022). TRIAC treatment improves impaired brain network function and white matter loss in thyroid hormone transporter *Mct8/Oatp1c1* deficient mice. *International Journal of Molecular Sciences, 23*(24), 15547.

Remerand, G., Boespflug-Tanguy, O., Tonduti, D., Touraine, R., Rodriguez, D., Curie, A., et al. (2019). Expanding the phenotypic spectrum of Allan–Herndon–Dudley syndrome in patients with *SLC16A2* mutations. *Developmental Medicine & Child Neurology, 61*(12), 1439–1447.

Schwartz, C. E., Peron, A., & Kutler, M. J. (2013). Snyder-Robinson Syndrome. In M. P. Adam et al. (Eds.), *GeneReviews*®. University of Washington, Seattle.

Siemes, D., Vancamp, P., Markova, B., Spangenberg, P., Shevchuk, O., Siebels, B., et al. (2023). Proteome analysis of thyroid hormone transporter Mct8/Oatp1c1-deficient mice reveals novel dysregulated target molecules involved in locomotor function. *Cells, 12*(20), 2487. https://doi.org/10.3390/cells12202487

Sriram, S., Shahid, N., Mysliwiec, D. D., Lichter-Konecki, U., Yatsenko, S. A., & Garibaldi, L. R. (2024). Late diagnosis of the X-linked MCT8 deficiency (Allan-Herndon-Dudley syndrome) in a teenage girl with primary ovarian insufficiency. *Journal of Pediatric Endocrinology and Metabolism, 37*(4), 371–374. https://doi.org/10.1515/jpem-2023-0070

Starks, R., Kirby, P., Ciliberto, M., & Hefti, M. (2018). Snyder-Robinson syndrome. *Autopsy & Case Reports, 8*(3), e2018031. https://doi.org/10.4322/acr.2018.031

Swiston, C. J., & Nash, D. L. (2018). Intermittent esotropia in 4 patients with Allan-Herndon-Dudley syndrome. *Journal of Child Neurology, 33*(8), 525–527. https://doi.org/10.1177/0883073818770597 PMID: 29714107

Van Geest, F. S., Meima, M. E., Stuurman, K. E., Wolf, N. I., van der Knaap, M. S., Lorea, C. F., et al. (2021). Clinical and functional consequences of C-terminal variants in MCT8: A case series. *Journal of Clinical Endocrinology & Metabolism, 106*(2), 539–553. https://doi.org/10.1210/clinem/dgaa795

Visser, T. J. (2013). Thyroid hormone transporters and resistance. *Endocrine Development, 24*, 1–10. https://doi.org/10.1159/000343695

Visser, W. E. (2021). Therapeutic applications of thyroid hormone analogues. *Annales d'Endocrinologie, 82*(3–4), 170–172. https://doi.org/10.1016/j.ando.2020.03.004

Wakabayashi, K., Osaka, H., Kojima, K., Imaizumi, T., Yamamoto, T., & Yamagata, T. (2021). MCT8 deficiency in a patient with a novel frameshift variant in the *SLC16A2* gene. *Human Genome Variation, 8*(1), 10. https://doi.org/10.1038/s41439-021-00142-0

Yiu, R. S., Ling, T. K., Ko, C. H., Poon, S. W., Poon, G. W., Wong, F. C., et al. (2023). Allan-Herndon-Dudley syndrome in Hong Kong: Implication for newborn screening. *Clinica Chimica Acta, 551*, 117621. https://doi.org/10.1016/j.cca.2023.117621

DISCLAIMER
This chapter is an extended version of the article published by the same author(s) in the following journal.
Asian Journal of Pediatric Research, 14(7): 79-85, 2024. DOI: 10.9734/ajpr/2024/v14i7368;
https://journalajpr.com/index.php/AJPR/article/view/368

Peer-Review History:
This chapter was reviewed by following the Advanced Open Peer Review policy. This chapter was thoroughly checked to prevent plagiarism. As per editorial policy, a minimum of two peer-reviewers reviewed the manuscript. After review and revision of the manuscript, the Book Editor approved the manuscript for final publication. Peer review comments, comments of the editor(s), etc. are available here: https://peerreviewarchive.com/review-history/5685