FORWARD

About the Foundation

The EBF3 HADDS Foundation was established in 2019 to promote awareness, invest in HADDS research, and to support & connect families and individuals living with Hypotonia, Ataxia, and Delayed Development Syndrome (HADDS), a rare neurodevelopmental syndrome caused by a mutation in the EBF3 gene on the 10th chromosome.

About the Understanding HADDS Education Packet

Since December of 2019, the EBF3 HADDS Foundation has worked to develop a comprehensive education packet for individuals living with HADDS and their families, the public, and the medical community. This packet is focused on understanding what HADDS is, the underlying genetics behind it, and the strategies and therapies designed to help individuals develop and thrive. Whether you or someone you care about has been diagnosed with HADDS, or you just want to understand more about the syndrome, our hope is that this resource can serve as a good starting point in understanding the diagnosis and how it presents. The Foundation would like to thank the medical subject matter experts and HADDS family contributors who provided their valuable expertise and experience in developing these materials. In addition to this material, additional information, links to published research, and other resources, can be found on HADDS.org in the "About" section. We will continue to update this education packet as we learn more about the syndrome through ongoing HADDS research and the shared experiences of our growing HADDS community. Developing additional education packets on various HADDS-related subjects is our goal in the future. If you're interested in contributing to these educational resource endeavors, please contact the EBF3 HADDS Foundation at info@hadds.org.

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HADD Syndrome Is Just A Trait...

It's no different than if you had asthma, diabetes or high blood pressure. It doesn't change the fact that they're our family, they're our loved ones and it certainly doesn't change the fact that they're superheroes to all of us. They're either fashion stars, equine champions, or musicians. They're some of the most loving, kind people you can find. Over the years you're going to hear us go into a lot of the research and scientific jargon updates, but I want us to remember that that's who they are. HADD Syndrome is just one trait that we're going to try to figure out so we can help them become the best superheroes they can be.

~Dr. Hsiao-Tuan Chao, HADDS Clinician & Researcher

I. EBF3-HADDS: Overview

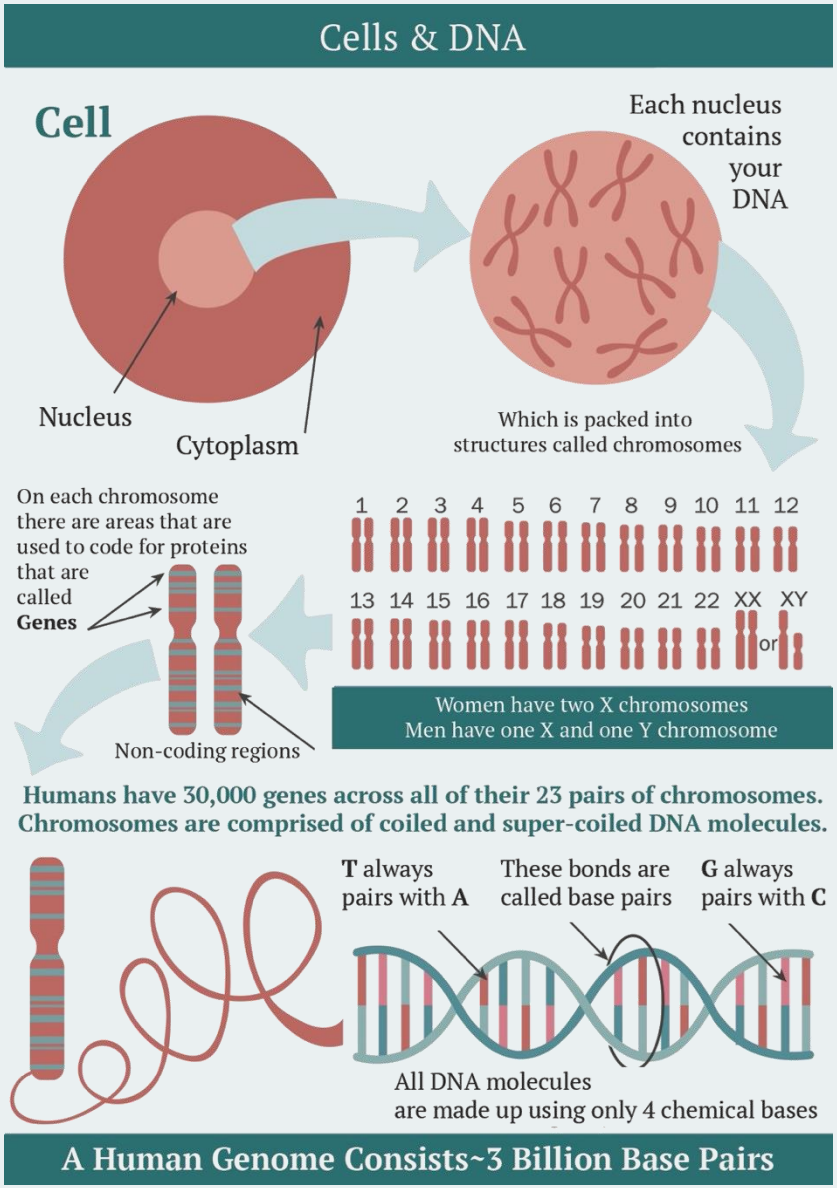
Dr. Hsiao-Tuan Chao

Dr. Hugo Bellen

Dr. Michael Wangler

Early **B**-Cell **F**actor **3** (EBF3) **H**ypotonia, **A**taxia, and **D**elayed **D**evelopment **S**yndrome (HADDS) is an autosomal dominant neurodevelopmental disorder, characterized by delayed motor and language development, variable effects on cognition, cerebellar ataxia, hypotonia, low muscle tone, distinct facial features, genitourinary abnormalities, and is often associated with underdevelopment of the cerebellum.[1] Dr. Hsiao-Tuan Chao, Dr. Hugo J. Bellen, Dr. Michael F. Wangler, and their colleagues co-discovered the syndrome in 2016 along with two other research teams.

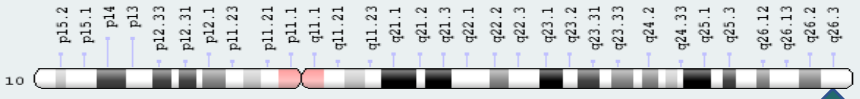
If you aren't familiar with these terms, you aren't alone! This info packet will cover the syndrome, terminology and its characteristics in detail.



Understanding Our DNA

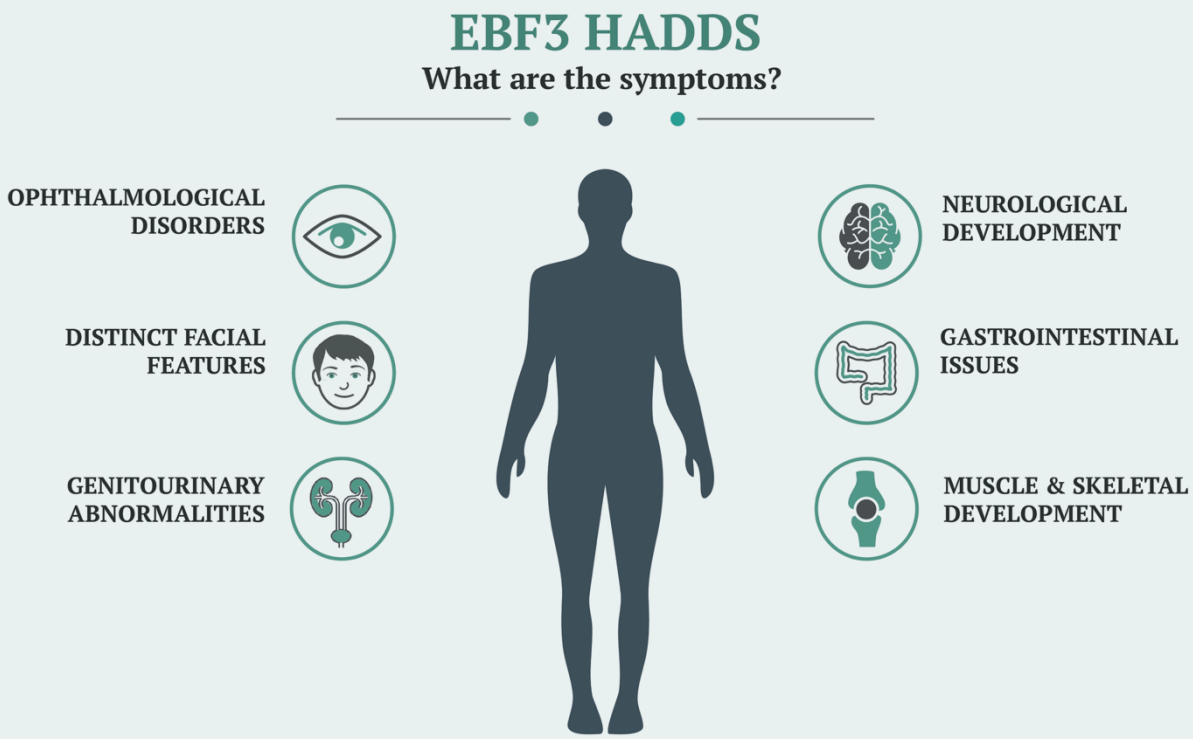
EBF3 HADDS is caused by a mutation in the gene Early B-Cell Factor 3 (EBF3), a master controller/regulator gene on the 10th chromosome, which is important for neurologic function. It's a transcription factor – which controls how many other genes are turned on or off (the building blocks of who you are) in cells. In particular it codes for the building of a protein that's needed for brain development and function. It's a very important gene that's found in an almost identical structure across many different species, such as fruit flies, which share almost 70% of the gene in common in humans. A mutation (or variant) in EBF3 that causes HADDS leads to the functional loss of one copy of EBF3. This loss reduces gene expression, so other genes are not being turned on or off like they should, and it consequently affects nervous system development, in particular a part of the brain known as the cerebellum. This mutation likely occurs at conception and manifests itself early in pregnancy.[2]

The cerebellum is located in the posterior region of the brain, and controls balance, coordination, motor control, attention, language (speech), cognition and social interaction (autistic-behaviors and lack of eye contact).



EBF3 Location: 10q26.3 is on the long arm of chromosome 10 at position 26.3.

How Does HADDS Present?



HADDS affects brain and other organ systems development, consequently affecting functionality, and leads to developmental delay and abnormalities in various body system areas, including neurological, genitourinary, gastrointestinal, ophthalmological, musculoskeletal, and facial features, among others. Some of the most prominent characteristics include speech delays, low muscle tone, strabismus of the eyes, developmental delay and balance issues.[3] However, each individual living with HADDS is unique -- not all features described in this packet may be present as it likely depends on the specific type of EBF3 mutation and how it's expressed.

Early Signs of HADDS during Infant / Toddler Years

- Lack of crying at birth, the first few months, or up to the first few years of life
- Inability to communicate hunger / difficulty breastfeeding during infancy
- Sleeping well and a rather inactive disposition when awake
- Head lag early on, may have been diagnosed early with Floppy Infant Syndrome (Hypotonia)
- Delays in lifting head up, sitting up independently, crawling and walking
- Not displaying many facial expressions, such as smiling or laughing
- Failure to meet height / weight goals
- Strabismus of the eyes
- Difficulty voiding, constipation, first UTIs and/or kidney infections
- As a result of these signs and symptoms, some young infants living with HADDS are given a diagnosis of Global Developmental Delay (GDD), Failure to thrive, and/or Cerebral Palsy early in life. Some toddlers may also be diagnosed with autism or other sensory disorders between 1 ½ - 3 years of age.

NEUROLOGICAL

- **Balance:** Impaired balance (ataxia) and coordination, making it difficult to walk
- **Motor:** Lack of muscle tone, and a floppy disposition in babies (hypotonia). For some, hypotonia may progress to hypertonia (primarily in the legs) as children reach puberty, leading to loss of mobility, increased pain and fatigue when walking for long periods of time or distances.
- **Speech:** Difficulty speaking (apraxia of speech), speech delays, dysarthria
- **Cognition:** Mild-to-moderate impairments or normally functioning
- **Attention:** Attention deficit/hyperactivity disorder (ADHD)
- **Social Behavior:** Autism-like behaviors / poor eye contact
- **Seizures:** Higher risk for seizures
- **Sleep:** Disruptive sleep cycles, sleep apnea
- **Brain anatomy:** May have underdevelopment of the cerebellum (cerebellar hemisphere and vermian hypoplasia)
- **High pain tolerance:** Especially as an infant/toddler, reduced pain sensitivity is common
- **Sensory issues:** Sensitivity to loud and/or unfamiliar sounds, bright lights or crowds
- **Stereotypes:** Self-stimulatory repetitive behaviors (stimming) such as physical movements, sounds, words and/or moving objects, neuropathic itching, compulsive eating of hair (trichophagia) and associated hair pulling (trichotillomania), self-injuring behavior[4]

NEUROLOGICAL

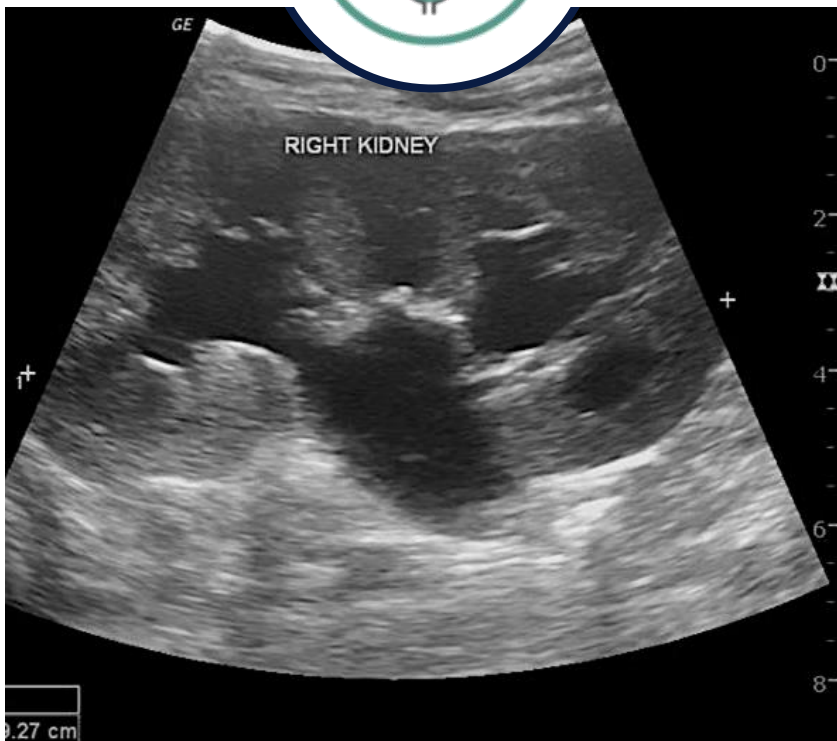
Other neurological / behavioral conditions reported with HADDS include:

- **Hydrocephalus:** An accumulation of cerebrospinal fluid (CSF) occurring within the brain. This typically causes increased pressure inside the skull which requires brain surgery to relieve (ETV or shunt)
- **Various types of seizures:** Absence seizures (petit mal) in children, tonic-clonic (grand mal) seizures, juvenile myoclonic epilepsy (JME) associated myoclonic seizures, febrile (fever-related) seizures
- **Sensory processing disorder (SPD)**
- **Auditory Sensory Defensiveness:** Reacting negatively, such as crying or screaming, in response to loud unexpected noises, aversion to crowded environments.
- **Developmental Coordination Disorder (DCD)**
- **Clonus:** Involuntary, rhythmic muscular contractions and relaxations
- May appear to ignore people or not respond to tickling, difficulty laughing
- **Tics:** Nose scrunching, shrugging shoulders, squinting, tongue clicking, clenching teeth
- **Intention tremors:** Intention tremors in hands/arms when engaging in fine motor skill activities
- **Difficulty regulating body temperature**
- **Unilateral Weakness:** One side of the body (eye, leg, arm, etc..) appears weaker than the other
- **Pathological demand avoidance (PDA):** An autistic tendency characterized by an overwhelming need to avoid or resist demands. Individuals with HADDS with PDA experience high anxiety levels and can feel that they are not in control
- **Learning:** For some children with HADDS, receptive language skills, memory and reading skills may be normal (or even above average) for their grade level. Music and use of technology are other strengths. However, mathematics tends to be more challenging for many with HADDS. ADHD may also be present and affect ability to focus in class.

GENITOURINARY

Common genitourinary traits primarily affecting the bladder and kidneys among many with HADDS include:

- **Cryptorchidism:** undescended testes
- **Underdeveloped external genitalia:** micropenis / decreased volume of labia
- **Urethral abnormalities**
- **Infections:** Recurrent urinary tract infections (UTIs) and/or kidney infections (pyelonephritis)
- **Backflow of urine from bladder to kidneys (vesicoureteral reflux):** Urine propelled back into ureters and kidneys with voiding
- **Bladder distention and Incomplete bladder emptying**
- **Hydroureter / hydronephrosis:** Excess urine causing distention, dilation of the ureters, kidneys
- **Urinary incontinence:** Prolonged / difficulty with potty training
- **Infrequent voiding or abnormal urine stream:** May have problems relaxing urethral sphincter resulting in difficulty voiding and intermittent stream
- **Neurogenic bladder dysfunction:** Bladder may not hold urine comfortably/under low pressure or empty effectively
- **Flank pain associated with the kidneys:** May signify kidney infection
- **Proteinuria:** Excess protein in the urine
- **Issues at puberty:** Some children may eventually outgrow bladder dysfunction or urinary incontinence, while for some children living with HADDS, urinary issues such as intermittent voiding may emerge at puberty. Others living with HADDS may have these issues across their lifespan.[5]
- **Bicornuate uterus (rare finding)**



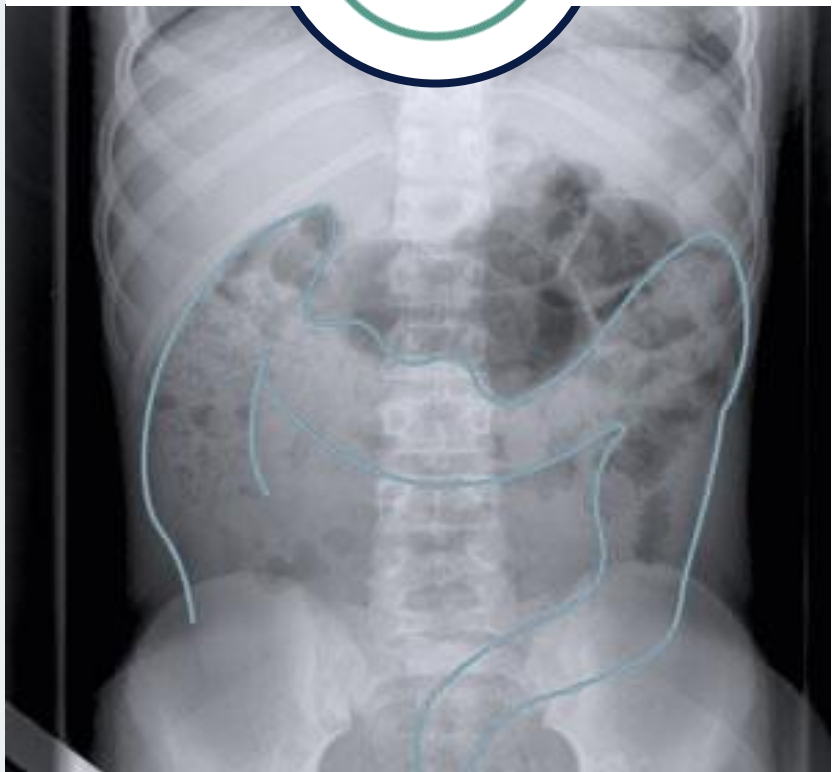
GASTROINTESTINAL

Common digestive system traits among many with HADDS include:

- **Constipation**: often chronic and severe, may be lifelong
- **Decreased motility:** hypotonia-related
- **Bowel incontinence:** can also be associated with constipation
- **Gastroesophageal reflux disease (GERD)**
- **Dysphagia:** Difficulty swallowing; Among many younger children living with HADDS, there may be difficulty eating solid foods, holding food in cheeks, silent aspiration with thin liquids, choking easily, stopping breathing when eating, tracheomalacia, difficulty with breastfeeding (suck-swallow-breath reflex difficulties), laryngeal penetration or pooling in the vallecula. For some, dysphagia may persist beyond early childhood or throughout life.[6]

Other gastrointestinal-related conditions reported among some with HADDS:

- **Failure to thrive:** Difficulty gaining weight, especially as an infant. Children with HADDS are often under the 50th percentile for height and/or weight on growth charts
- **Difficulty communicating hunger**
- **Low functioning bowels / megacolon**
- **Delayed gastric emptying**
- **Gastroparesis:** Stomach cannot empty itself of food in a normal fashion. Symptoms include heartburn, nausea, vomiting, and feeling full quickly when eating
- **Sialorrhea:** Heavy drooling, excess salivation

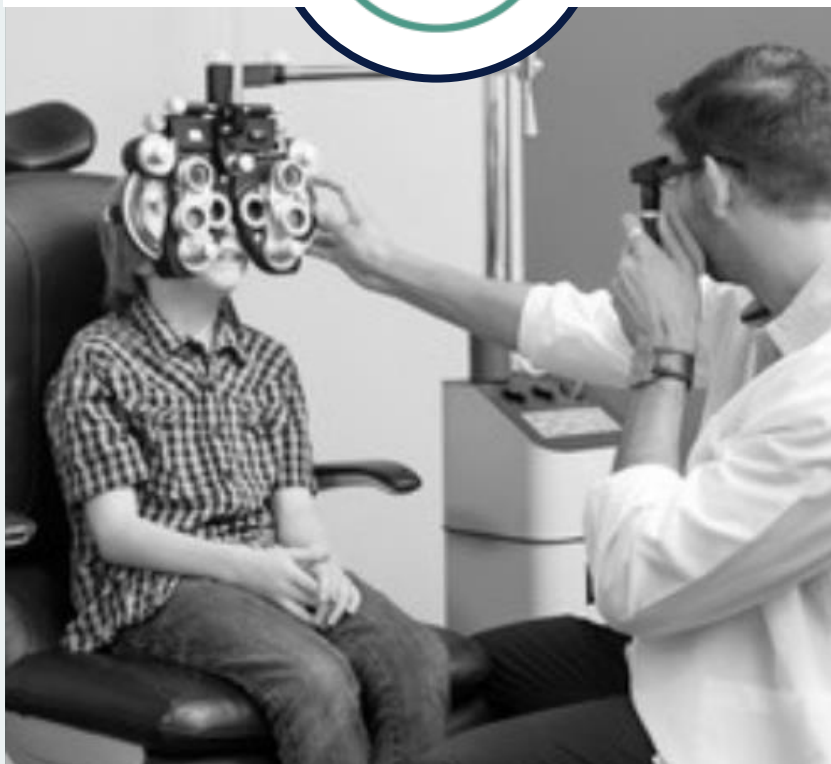


OPHTHALMOLOGY

- **Strabismus:** Abnormal alignment of the eyes. Forms of strabismus reported include **esotropia**, where one or both eyes turn inward, and **amblyopia** (lazy eye) in one or both eyes.

Other common ophthalmological traits among some with HADDS include:

- **Myopia:** Near-sightedness
- **Hyperopia:** Far-sightedness
- **Astigmatism:** Leading to blurry or distorted vision, eyestrain, headaches, trouble seeing at night

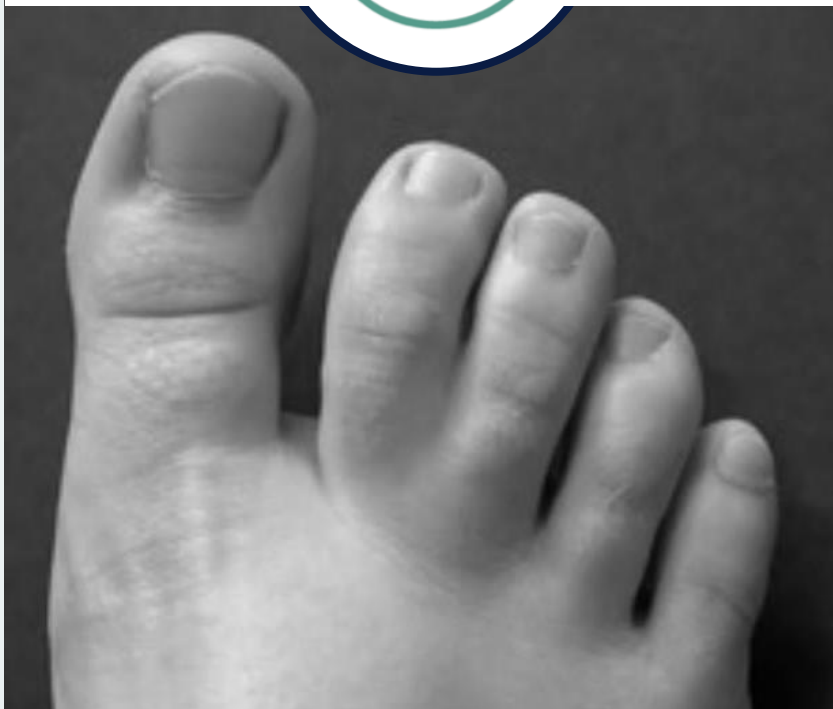


MUSCULOSKELETAL

- **Hypotonia:** Poor muscle tone, making it difficult to make coordinated movements such as walking. For some, hypotonia may progress to the opposite extreme, hypertonia (high muscle tone) particularly in the legs, as children reach puberty. This can lead to loss of mobility, increased pain, and fatigue when walking for long periods of time or distances.
- **Laryngomalacia:** Lack of muscle tone (hypotonia) in the airway. If sedated for surgery, MRI or other testing, laryngomalacia can put individuals with HADDS at an increased risk for laryngospasm, causing an obstruction of the airway, and could become a life-threatening situation.
- **Scoliosis:** Sideways curvature of the spine
- **Dystonia:** Involuntary muscle contractions that cause repetitive or twisting movements.
- **Hands and feet:** May be smaller than average
- **Stature:** Individuals with HADDS may be of shorter than average height
- **Infancy delays:** Poor head control in infancy, slower to reach crawling, sitting up, walking milestones[7]

Other conditions reported among some with HADDS:

- **Broken bones:** Due to ataxia and hypotonia-related balance and control challenges, many children living with HADDS are at increased risk for sudden falls, leading to clavicle fractures or fractures of bones in the arms or hands typically.
- **Torticollis:** Condition in which the neck muscles contract, causing the head to twist to one side. Positional torticollis is seen in infancy due to the low muscle tone.
- **Foot abnormalities:** Bilateral talipes (clubfoot), syndactyly (fused digits), bent or curved-in toes
- **Clinodactyly:** Bend of the fifth digits in the hands
- **Pectus excavatum:** Sunken, concave chest



UNIQUE FACIAL CHARACTERISTICS

- **Hypomimia:** Reduced facial expression, such as difficulty smiling (often appears as a grimace). However, facial expressions of emotion can improve as children get older
- **Dysmorphisms:** Mild-to-moderate distinct facial features such as
  - Long face
  - Tall and/or pronounced forehead
  - High/wide nasal bridge
  - Deep philtrum
  - Straight eyebrows
  - Short and broad (prominent/prognathic) chin
  - Hypertelorism
  - Synophrys (fusion of eyebrows above bridge of nose)
  - Deep-set eyes
  - Triangular face
  - Small ears
  - Facial asymmetry
  - Highly arched palate and crowded teeth[8]

IMMUNE SYSTEM

- While individuals with HADDS are at higher risk for UTIs and kidney infections (pyelonephritis) due to neurogenic bladder dysfunction, reflux, and intermittent catheterization, their immune system in general appears to function quite normally.

II. HADDS RESEARCH: HADDS Timeline

2010-2012: Clinical Whole Exome Sequencing introduced

October 2015: NIH's Undiagnosed Disease Network (UDN), other studies on EBF3 HADDS begin

Spring 2016: Baylor College of Medicine, Texas Children's Duncan Neurological Research Institute begin work on studying EBF3

January 2017: EBF3 HADD Syndrome discovery published in 3 distinct reports in the American Journal of Human Genetics as case studies of 21 patients.

Summer 2017: EBF3 neurodevelopmental syndrome was named HADDS (Hypotonia, Ataxia and Delayed Development Syndrome) by Mendelian Naming System

June 2017: The first HADD Syndrome clinic established at Texas Children's Hospital's Blue Bird Neurology Clinic by Dr. Hsiao-Tuan Chao and Dr. Michael Wangler, to improve understanding of the condition's unique features and comorbidities and provide care and medical knowledge for HADDS families.

October 2018: HADDS Clinical Study receives IRB approval, begins at TX Children's Hospital and Duncan Neurological Research Institute

February 2019: EBF3 HADDS Foundation established

June 2019: HADDS.org and HADDS Shop established, driving awareness and the start of fundraising for research, conference and family support

July 2019: 1st International HADDS Conference hosted at Texas Children's Hospital in Houston, TX with over 100 attending and 15 families attending via live stream worldwide.

November 2019: HADDS Plaid Ribbon & Clothing Awareness Campaign introduced

February 2020: HADDS Awareness Month established

March 2020: $60,000+ raised in the first year towards research, travel grants for families & conferences

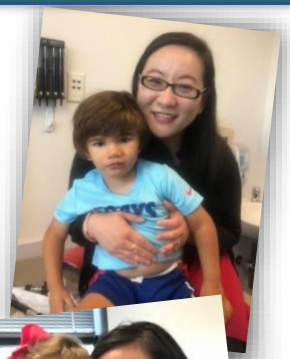
October 2020: 1st HADDS In Motion Run

HADDS LAB & CLINIC

The epicenter of EBF3 HADDS discovery, expertise and ongoing research globally is in Houston, TX, U.S., at the Jan & Dan Duncan Neurological Research Institute (NRI) (nri.texaschildrens.org) – a joint endeavor between Texas Children's Hospital and Baylor College of Medicine, which opened in 2010. Some of the leading basic research and clinician scientists in the world have joined forces and are committed to discovering new neurological diseases, their underlying causes, and pursuing possible therapy breakthroughs. It's a place that's bridging research and clinical medicine, through funding support from the American Academy of Neurology, NIH Director's Common Fund for High-Risk High-Reward, Burroughs Wellcome Fund, Child Neurology Society Research Foundation, Pediatric Epilepsy Research Foundation, and the McNair Medical Institute at the Robert and Janice McNair Foundation. It was there in December 2016 that Dr. Hsiao-Tuan Chao, Dr. Hugo Bellen and Dr. Michael Wangler co-discovered the syndrome (sciencedaily.com/releases/2016/12/161223115920.htm). Today at Dr. Chao's HADDS Laboratory at the NRI, she and her dedicated team of investigators continue to focus on better understanding the neurological mechanisms behind this syndrome through fruit fly and mice model studies, along with on-going clinical evaluations and human genotype-phenotype studies.

When not in the HADDS lab, she and her geneticist colleague, Dr. Michael Wangler, can be found at Texas Children's Hospital's nationally recognized Blue Bird Neurology clinic (texaschildrens.org/departments/neurology), where they host a monthly HADDS clinic. This clinic is the first to be established worldwide specifically for HADDS. There, children from across the U.S. and internationally come to be evaluated annually by these two subject matter experts. Clinical evaluation and assessment of medical records/imaging of patients with HADDS helps to better understand its most common characteristics, leading to a more well-informed medical community, empowered to diagnose and treat HADDS earlier in other children globally. These evaluations are also essential for aiding their ongoing research in the HADDS Lab. In return they pass along their expertise to help care for and educate patients and families living with HADDS.

HADDS CLINIC & LAB CONTACT INFORMATION





HADDS Clinic:

Blue Bird Circle Clinic for Pediatric Neurology, Texas Children's Hospital
6701 Fannin St, Houston, TX 77030

If interested in being seen at the HADDS Clinic by Dr. Chao (pediatric neurologist and head of the HADDS Lab at the NRI) and Dr. Michael Wangler (geneticist), please contact the Blue Bird Neurology Clinic (832-822-5046) and request to speak with Marcus Brisker who can assist with the appointment.

Initial evaluation appointments are typically 2 hours in duration (1 hour with Dr. Chao / 1 hour with Dr. Wangler). Recommended annual re-evaluation appointments are 1 hour in duration (30 min with Dr. Chao / 30 min with Dr. Wangler).

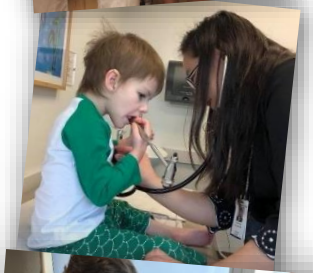
A clinical evaluation annually is recommended, as Drs. Chao and Wangler are subject matter experts with the experience/clinical expertise to assess individuals with HADDS properly. If travel to Houston is not a viable option, send them an update via email (chao-lab@bcm.edu) or phone call to their research coordinator (832-826-0454) with copies of medical records and imaging studies annually. For coordination of care, if you grant permission to your hometown physician, they're welcome to consult with Dr. Chao and Dr. Wangler and can send them reports to review.

Chao's "HADDS Lab":

Jan & Dan Duncan Neurological Research Institute, Texas Children's Hospital & Baylor College of Medicine. Address: 1250 Moursund St, Suite 925, Houston, TX 77030

If interested in learning more about ongoing HADDS research at the Chao "HADDS Lab" and how to participate in EBF3 HADDS Clinical Studies, you can email chao-lab@bcm.edu or call 832-826-0454. They can refer you to the Blue Bird Neurology HADDS Clinic scheduler and explain the research study.

Dr. Chao's Research Bio: nri.texaschildrens.org/faculty/hsiao-tuan-chao-md-phd
Dr. Chao's Lab Website:
https://www.bcm.edu/research/labs-and-centers/faculty-labs/hsiao-tuan-chao-lab
Dr. Wangler's Research Bio: https://nri.texaschildrens.org/faculty/michael-wangler-md


HADDS RESEARCH GOALS

I. Understand the EBF3 Gene and Mutation characteristics:

1.) Natural History Study – to study as many HADDS individuals as possible in order to gain a longitudinal understanding of HADDS over the lifespan
2.) How specific EBF3 gene changes (genotype mutations/variants) relate to different physical & neurological manifestations (phenotype variation) in the HADDS population
3.) Complications of HADDS and comorbidities

II. Understand the underlying genetic mechanism of EBF3 (using fruit fly studies):

1.) EBF3 and nervous system development
2.) Genetic pathways and target genes
3.) How to bypass the effects of EBF3 mutations

III. Precision medicine (using mouse models):

1.) Neural circuits and brain development
2.) Vulnerable neuron types and brain regions
3.) Genetic pathways and target genes[9]

The long-term goal is to apply EBF3 research discoveries towards gene therapy solutions that could help manage symptoms for those living with HADDS

EBF3 HADDS PUBLICATIONS

There are currently 9 studies that have been published. Selected publications are below for reference. As funding helps support continued research, the knowledge base will continue to grow!

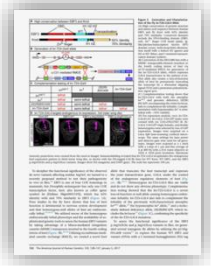
1/5/2017 - A Syndromic Neurodevelopmental Disorder Caused by De Novo Variants in EBF3. American Journal of Human Genetics: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5223093/

1/5/2017 - De Novo Mutations in EBF3 Cause a Neurodevelopmental Syndrome. American Journal of Human Genetics: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5223060/

1/5/2017 - Mutations in EBF3 Disturb Transcriptional Profiles and Cause Intellectual Disability, Ataxia, and Facial Dysmorphism, American Journal of Human Genetics: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5223027/

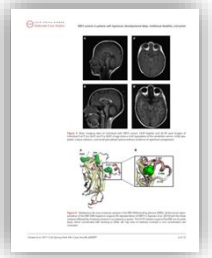
5/3/2017 - Novel de novo variant in EBF3 is likely to impact DNA binding in a patient with a neurodevelopmental disorder and expanded phenotypes: patient report, in silico functional assessment, and review of published cases. Cold Spring Harbor Molecular Case Studies: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5411688/

10/9/2017 - Whole Gene Deletion of EBF3 Supporting Haploinsufficiency of This Gene as a Mechanism of Neurodevelopmental Disease. Frontiers in Genetics: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5640723/



11/21/2017 - De novo variants in EBF3 are associated with hypotonia, developmental delay, intellectual disability, and autism, Cold Spring Harbor Molecular Case Studies: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5701309/pdf/TanakaMCS002097.pdf

12/25/2019 - Cylindrical spirals in two families: Clinical and genetic investigations, Neuromuscular Disorders: https://www.nmd-journal.com/article/S0960-8966(19)31233-7/fulltext



12/29/2020 - Integrated phenotypic and mutational approach defines EBF3-related HADD syndrome genotype-phenotype relationships: https://www.medrxiv.org/content/10.1101/2020.12.07.20238691v2

3/26/2022 - An Integrated Phenotypic and Genotypic Approach Reveals a High-Risk Subtype Association for EBF3 Missense Variants Affecting the Zinc Finger Domain: https://www.hadds.org/_files/ugd/9967df_58f6dfaded454df9b3808025482067be.pdf

For more information visit: https://www.hadds.org/research

HADDS RESEARCH

THE VALUE OF HADDS RESEARCH

- By studying rare conditions like HADDS, we can help millions who are affected by Autism, ADHD, seizures or other more common conditions with overlapping traits
- Helps us understand other rare conditions that are similar "cousin" syndromes to HADDS
- Natural history studies of a large sample size of HADDS patients are necessary for FDA approval process of any treatments[10]
- Improves recognition by the medical and scientific communities
- Improves access to therapies and state or federal resources

SYNDROMES SIMILIAR TO HADDS

- **Floating Harbor Syndrome:** Caused by a de novo mutation in SRCAP gene. Characteristics include strabismus, renal and genitourinary abnormalities, language delay https://ghr.nlm.nih.gov/condition/floating-harbor-syndrome
- **Myhre Syndrome:** Caused by de novo mutations in SMAD4 gene. Characteristics include short stature, strabismus, laryngeal stenosis, hypotonia, ataxia[11] https://ghr.nlm.nih.gov/condition/myhre-syndrome

III. THE GENETICS OF HADDS

GENETIC TESTING TO CONFIRM A HADDS DIAGNOSIS

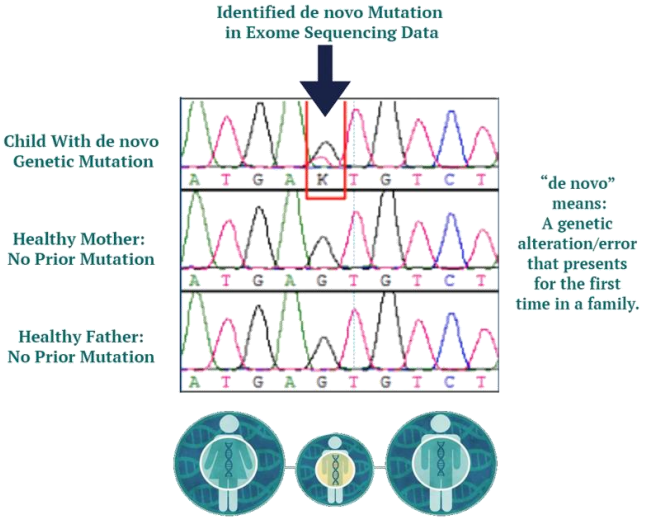
If a parent and/or medical provider suspects HADDS based on signs and symptoms, genetics providers recommend two genetic tests to rule out other genetic conditions that present similarly to HADDS and to confirm a HADDS diagnosis:

- Chromosome Microarray Analysis (CMA): To rule out large chromosome abnormalities.
- Whole Exome Sequencing (WES): Detects "misspelled" DNA strands within the most important parts of the genome (the coding parts known as "exons"). This can detect variants in the EBF3 gene to confirm a HADDS diagnosis.
- Some gene panels for ataxia syndromes now include the EBF3 gene.
  In addition to testing the child, parental testing may be recommended to help interpret uncertain results and to provide accurate recurrence risk information. The vast majority of the time, parental testing results will be negative (normal), indicating that the EBF3 mutation causing HADDS occurred for the first time in the child – what's known as a "de novo" mutation or "new event."[12]

CAUSES OF DE NOVO MUTATIONS

While radiation exposure (UV and x-rays) and chemical exposures can cause DNA mutation, by far the biggest factor is increased DNA replication as we age, which increases the risk of random, new "de novo" errors in the DNA.

Advancing age of the mother can increase the risk for large, chromosome abnormalities (i.e. EBF3 deletions, rearrangements), while advancing age of the father can increase the risk of EBF3 point mutations (i.e. missense or misspelling). However, most of the time, these changes happen by chance and are unrelated to a parent's age or environmental exposures. There is often nothing that parent could have or should have done differently before or during the pregnancy to reduce the chances of having a child with HADDS. It is no one's fault. Parents can't control or prevent "de novo" mutation events, and diet/exposures have limited impact.[13]



THE GENETICS OF HADDS

VARIOUS TYPES OF EBF3 MUTATIONS

- **Missense:** Point mutation in which a single nucleotide change (i.e. cytosine to thymine) results in a codon that codes for a different amino acid, leading to a change in protein (observed in 50% of HADDS individuals so far).
- **Nonsense (stop):** Point mutation in a sequence of DNA that results in a premature stop codon, and in a truncated, incomplete, and usually nonfunctional protein product.
- **Splicing:** A mutation that inserts, deletes or changes a number of nucleotides in the specific site at which splicing takes place during the processing of precursor messenger RNA into mature messenger RNA.
- **Indel / Frameshift:** A mutation caused by **in**sertions or **del**etions of a number of nucleotides in a DNA sequence that is not divisible by three. Due to the triplet nature of gene expression by codons, the insertion or deletion can change the reading frame, resulting in a completely different translation from the original.
- **Gene Deletion:** A mutation where the entire gene sequence is absent, resulting in a 50% reduction in EBF3 protein expression.[14]

INTERPRETING GENETIC TEST RESULTS

The genetic results give the location of the variant (spelling change) in two ways for this example:

c. 1345 A>G (p.Phe448Tyr)

1.) The specific DNA code and location of change:

Example: "c._____" (i.e. c.1345 A>G) In this example, at coding nucleotide position number c.1345, a "A" (adenine) was changed to a "G" (guanine)

2.) The specific amino acid (the building blocks of proteins) change:

Example: "p. _____" (i.e. p. Phe448Tyr) In this example, at codon (each codon codes for a different amino acid) number 448, the amino acid Phenylalanine was changed to Tyrosine[15]

GENETICS & ADDITIONAL CHILDREN

THE LIKELIHOOD OF HAVING ANOTHER WITH HADDS

Nearly all cases of HADDS are caused by a random, new, "**de novo**" point-mutation change at conception in one copy of the EBF3 gene and was not inherited from either parent. Therefore, the risk of having another child with HADDS is very low **(< 1%)** if genetic testing confirms the parents did not have the EBF3 mutation themselves.

However, if a parent has an EBF3 mutation in a portion of their blood (or saliva) cells when tested, this is known as **mosaicism**. If the EBF3 variant is in their sperm or eggs cells (known as **gonadal/germline mosaicism**), then the risk of having another child with HADDS may be higher **(>1% risk)**. A geneticist may be able to assess the risk based on individual parental testing results.[16]

PRENATAL TESTING OPTIONS FOR HADDS

Invasive prenatal testing: Chorionic villi sampling (CVS) during the 1st Trimester (10-14 weeks) or Amniocentesis during the 2nd Trimester (15-20 weeks) can be performed during the pregnancy to screen for HADDS.

Routine chromosome analysis tests are routinely performed, but this test will NOT detect HADDS. Instead, your genetic counselor will need to specifically request either: an EBF3 genetic test or Known Familial Mutation Analysis. You must confirm that a lab is willing to perform this test and they may require a blood sample of the child to ensure they are able to identify the mutation in their lab.

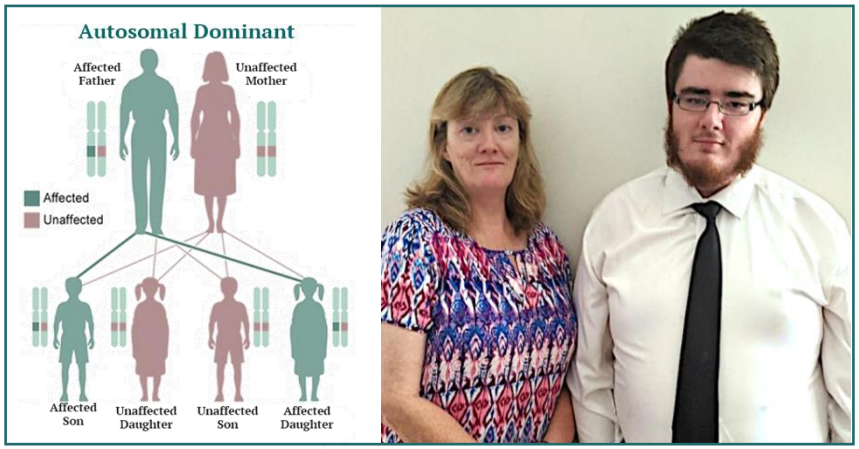
Non-Invasive Prenatal Testing (NIPT): Now available to pregnant women who do not want invasive techniques. However, it is NOT currently available to screen for HADDS, though it may be in the future.[17]

GENETIC INHERITANCE & PREDICTION

HADDS – A GENETIC MUTATION

Autosome: The mutation is on an "autosome" (in the case of this syndrome, on the 10th chromosome) which is one of 22 non-sex chromosomes. Therefore, it affects both boys and girls, with relatively equal prevalence.

Dominant: Individuals with the mutation always express the trait (even though it's only on one of the two copies of the gene inherited from their parents).[18]



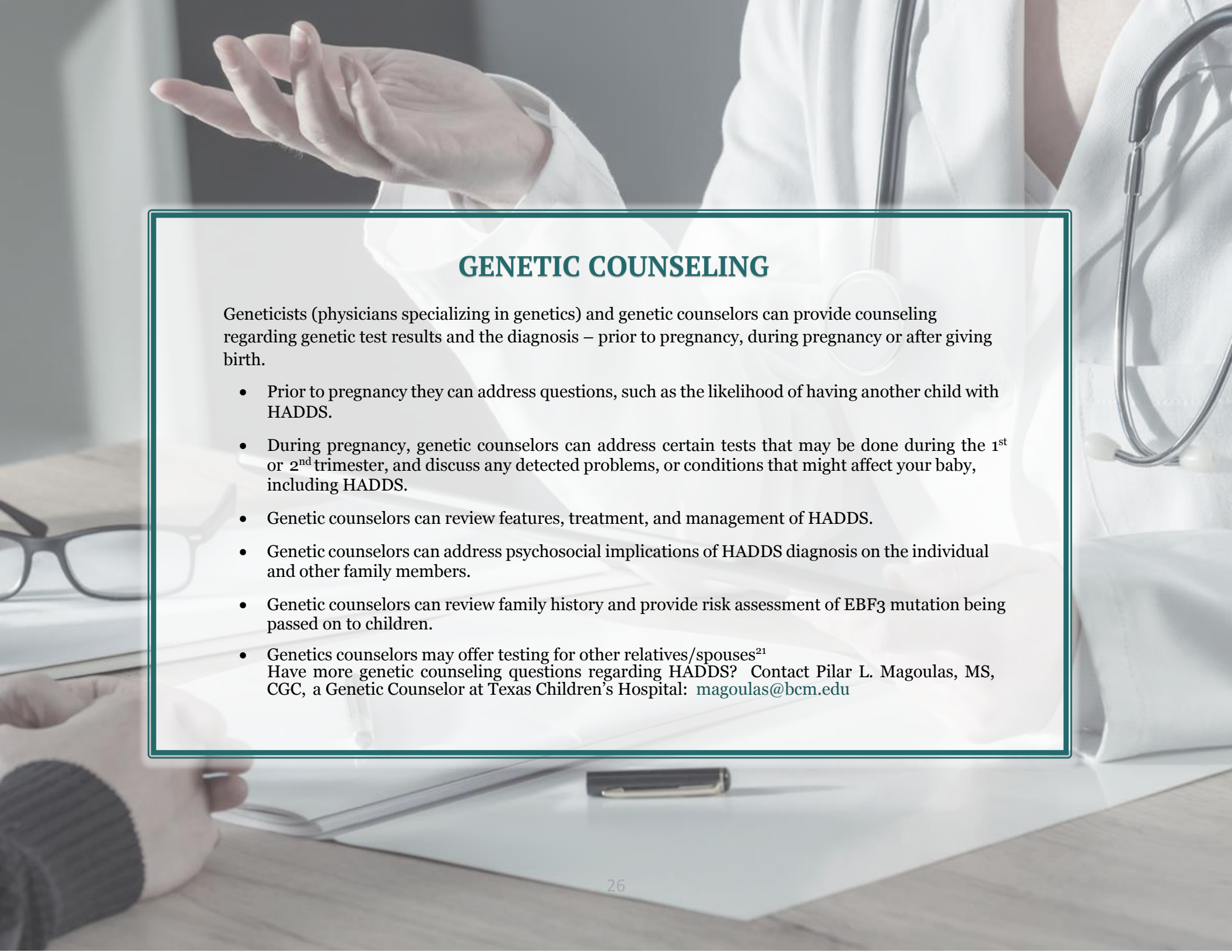
Louise and Denholm Willmer of Toorbul, Australia are an example of an individual with HADDS passing the EBF3 gene variant to her child. Her firstborn son is unaffected.

INHERITANCE FROM A PARENT WITH HADDS

Since HADDS is an autosomal dominant condition, individuals with HADDS have one normal EFB3 gene copy and one mutated EBF3 gene copy. However, they only pass one copy of the gene on at conception. Thus, there is a **50% chance** with each pregnancy that a child will inherit the EBF3 mutation from a parent with HADDS.[19]

GENETIC PREDICTION OF PROGNOSIS

The type of EBF3 mutation may predict the severity of the symptoms, although less than 100 children have been evaluated by HADDS researchers internationally so far. Early findings indicate that children with a "missense" (a change in one letter – i.e., from adenine to guanine or cytosine to thymine) generally may display milder symptoms of the condition than an individual who has a deletion. However, it's unknown how specific variant mutations cause differences in severity of features. A more specific prognosis of how a child's clinical features such as physical and behavioral characteristics (phenotype) is expressed from the underlying specific genetic mutation on the EBF3 gene (genotype) will require continued investigation of more individuals with HADDS, in order to identify clearer trends.[20]



GENETIC COUNSELING

Geneticists (physicians specializing in genetics) and genetic counselors can provide counseling regarding genetic test results and the diagnosis – prior to pregnancy, during pregnancy or after giving birth.

- Prior to pregnancy they can address questions, such as the likelihood of having another child with HADDS.
- During pregnancy, genetic counselors can address certain tests that may be done during the 1st or 2nd trimester, and discuss any detected problems, or conditions that might affect your baby, including HADDS.
- Genetic counselors can review features, treatment, and management of HADDS.
- Genetic counselors can address psychosocial implications of HADDS diagnosis on the individual and other family members.
- Genetic counselors can review family history and provide risk assessment of EBF3 mutation being passed on to children.
- Genetics counselors may offer testing for other relatives/spouses[21]
  Have more genetic counseling questions regarding HADDS? Contact Pilar L. Magoulas, MS, CGC, a Genetic Counselor at Texas Children's Hospital: magoulas@bcm.edu

"When a Flower doesn’t bloom,

you fix the environment in which it grows."

~Alexander Den Heijer

IV. TESTING, TREATMENT & THERAPIES

Early detection, testing, treatment and consistent therapy is important for those living with HADDS to reach their full potential. Caregivers and medical providers should consider referrals to medical specialists and therapists in a variety of areas, including a neurologist, urologist & nephrologist, gastroenterologist, ophthalmologist, geneticist and genetic counselor, nutritionist/dietician, physical therapist, speech therapist, occupational therapist, and ABA therapist.

GETTING ORGANIZED

When navigating many medical and therapy appointments every week or every month, getting organized (or re-organized) early on is a great way to prevent feeling of burnout. Here are a few general tips suggested by many parents and caregivers:

- Use a large written monthly calendar or dry erase board with color-coded appointments written out by day for the upcoming month or reminders planned out for when to call to schedule follow-up appointments.
- Use the google calendar app (or another app) on phone to keep track of upcoming appointments/get reminders.
- Have a bag, designated binder or expanding file folder for school/IEP, one for medical appointments, one for therapies.
- Use an electronic file with info that can be easily pulled from laptop or phone if at appointments (i.e., google drive).
- Develop a running "Medical / Therapy History Timeline" word document that you can quickly email or give hardcopies to new providers and therapists. This can save time at appointments, so you don't have to repeat lengthy medical histories at each appointment. Add notes /dates regarding previous appointments, hospital stays, infections, testing, scans/imaging, surgeries, developmental milestones, when therapies began or changed, etc.
- If possible, schedule appointments / therapies on the same days/times each week to ensure a predictable routine.
- If your child's hospital system and/or insurance provider offers it, take advantage of using a Case Manager, who is typically a nurse or health care administrative advocate who can help coordinate the multi-disciplinary nature of your child's needs. They can help schedule appointments, oversee referrals/consults, insurance paperwork, etc.
- Seek out a trusted POC at the insurance company who knows your child's situation and you can rely on to call or email to expedite authorizations, billing snafus, etc.

NEUROLOGY TESTING & TREATMENT

NEUROLOGY TESTING & TREATMENT

Neurological Symptoms & Maintenance:

- **Initial evaluation/ re-evaluations:** If a HADDS diagnosis is suspected or confirmed, a referral to a neurologist for initial evaluation and consistent re-evaluation appointments to assess for progress is indicated.
- **Imaging:** Radiographic imaging (such as MRI, CT scans, etc.) of the brain and spinal cord to assess for underdevelopment of the cerebellum (cerebellar-vermian hypoplasia), hydrocephalus and tethered-cord. ******Laryngomalacia Note:*** Those living with HADDS may have a lack of muscle tone in the airway, known as laryngomalacia, which increases the risk of laryngospasm/cardiac arrest during sedation/upon extubating for surgery, MRI or other testing. Inform physicians, surgeons and anesthesiologists of their increased risk at pre-sedation appointments so providers can weigh the risk and benefits of sedation, take proper extra precautions and consider alternatives (such as conscious, fast MRI).***
- **Hypotonia / Ataxia evaluation:** Neurology evaluation for lack of muscle tone (hypotonia), impaired balance (ataxia), prescription/referrals/recommendations for orthotics, braces, walkers, wheelchairs and physical therapy.
- **Neuropsychology evaluation:** To assess for autism, ADHD, cognitive/intellectual delays, speech delays, with referral for speech therapy, occupational therapy and/or applied behavior analysis (ABA) therapy as needed – the earlier therapies begin, the better.
- **Seizures:** Determine if an electroencephalogram (EEG) is warranted, to assess for abnormal electrical activity in the brain to have a baseline to compare to and to rule out epilepsy. Also, if an individual has a seizure, a neurologist will often order an EEG as part of follow-up treatment.
- **Stand-by Seizure medications:** Discuss possible increased risk for febrile seizures and determine if prophylactic stand-by medication (Children's Tylenol or Motrin, Rx Diastat [Diazepam]) is warranted and have all caregivers acquire training in how to react in the event a seizure event. Ensure these meds are always accessible by including in a child's diaper bag and have another set of medications with the child's school nurse to give in the event of a high fever and/or febrile seizure.
- **Sleeping difficulty:** If difficulty sleeping, a neurological evaluation and possible referral for a sleep study may be indicated to assess for sleep apnea.
- **Audiology exam:** Referral for hearing test to rule out hearing difficulties, which can often lead to speech delays and difficulties in young children.

NEUROLOGY TESTING & TREATMENT

At-home Recommendations from HADDS Families:

- **Neurological itching:** Wilbarger protocol for sensory integration--brushing the body with a small surgical brush throughout the day (nationalautismresources.com/the-wilbarger-protocol-brushing-therapy-for-sensory-integration), ice cubes, cold compress or towels applied to area, baths, joint compression, chiropractor evaluation

- **Sleep difficulty:** Melatonin, or time-release Melatonin HP (to help individuals go to sleep and stay asleep through the night), Rx Clonidine (extended release), bed tent to ensure safety (The Safety Sleeper bed --Medicaid may cover), weighted blanket, weighted stuffed animals/vests (from Manimo), blackout curtains, white noise machine, essential oils, magnesium powder, epsom bath salts to increase magnesium at night, or L-tryptophan. ***Consult with medical providers prior to any medication use.***
- **Sleep apnea:** Sleep study, evaluation for possible removal of tonsils (tonsillectomy), removal of adenoids (adenoidectomy), possible CPAP machine to sleep with if diagnosed with moderate-severe sleep apnea.
- **Ataxia:** Theratog and weighted vests have been recommended.
- **ADHD:** Rx Ritalin or Rx Adderall, neurofeedback, Rx Focalin (consult with medical providers first)

- **Soft-shell Helmet use:** A soft helmet can be used to protect against head injuries caused by falls while learning to walk and run (especially while at school, away from parental support). Often therapists or medical providers can provide a referral to get a child fitted for a helmet. Danmar over-the-counter soft helmets are recommended.
- **Cuts:** Due to frequent falls, HADDS children are more prone to cuts. Many have found liquid Band-Aids more effective at promoting healing than traditional Band-Aids that children would prefer to pull off.

- **Hair pulling:** Some have had success in using a toy doll for children to pull the doll's hair instead
- **Loud/unfamiliar/trigger sounds:** Ear plugs, noise-cancelling headphones/ ear protectors
- **Preventing putting non-edible objects in mouth:** teething toys on pacifier clips
- **Hypertonia:** For some, hypotonia may progress to hypertonia as children get closer to puberty, making it difficult and fatiguing to walk for long periods of time and distances. Botox, consistent physical therapy, aquatic therapy, and possible use of AFOs are important to combat tightness in muscles.

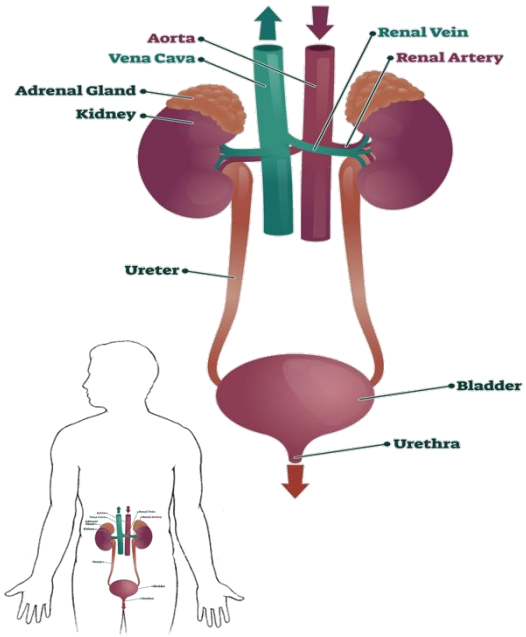
- **Behavioral issues:** Defiance or screaming tantrums, to the extent of pathological demand avoidance (PDA) can be an issue. Rest, maintaining a good sleep schedule and limited sensory exposure are good techniques to prevent. Other suggestions include positive reinforcement, time-outs, developing a calming routine can be helpful in these situations. For chronic behavioral issues, a psychological evaluation, developmental pediatrics evaluation, or counseling for behavioral/mood conditions such as ADHD are effective solutions.

UROLOGY & NEPHROLOGY TESTING & TREATMENT

UROLOGY & NEPHROLOGY TESTING & TREATMENT

Neurogenic bladder is common within the HADDS community. Neurogenic bladder is the name given to a number of urinary conditions in people who lack bladder control due to brain, spinal cord or nerve problems. The condition typically results in problems with storing urine under safe conditions and effective emptying of the bladder. Individuals living with HADDS are encouraged to get an initial evaluation and subsequent regular follow-up evaluations with a urologist (and often in coordination with a nephrologist). Evaluations typically begin with a history, physical examination and a **renal/bladder ultrasound** to check for bladder distention and dilation of the ureters/kidneys (hydroureteronephrosis). Based on a patient's history and imaging results, other tests prescribed by a urologist and/or nephrologist may include:

- Basic labs (urine analysis, CBC, chemistries) to assess creatinine levels, among others which assesses overall kidney function.
- Voiding studies to assess how the bladder functions and if any vesicoureteral reflux is occurring. These studies can include:



- **Uroflow/Post Void Residual:** This test can determine the strength and pattern of the urine stream and residual urine in the bladder after voiding; used in older children who can void on demand.
- **Electromyography (EMG)**: A non-invasive way to assess the pelvic floor muscle function while voiding.
- **VCUG**: This study can help detect if an individual is refluxing urine back up into the kidneys during urination, which increases the risk of kidney infection and kidney scarring. It's indicated for children with a history of urinary tract infections with a fever (a sign of kidney infection).
- **Urodynamic Study**: To assess for neurogenic bladder dysfunction. High pressure in the bladder and urinary tract infections with fevers can cause kidney damage. This study can detect dyssynergy between the bladder and urethral sphincter – while the bladder contracts with voiding, the pelvic floor should relax, not tighten.
- **Nuclear Medicine Scan (DMSA)**: A DMSA is indicated for those with frequent urinary tract and/or kidney infections. This scan can show how much permanent scarring there is in the kidneys.
- **MRI (magnetic resonance imaging) of the Spine**: To check for a tethered spinal cord (particularly in the lumbar region of the spine) which can be an underlying contributing factor for neurogenic bladder dysfunction in some cases.[22]

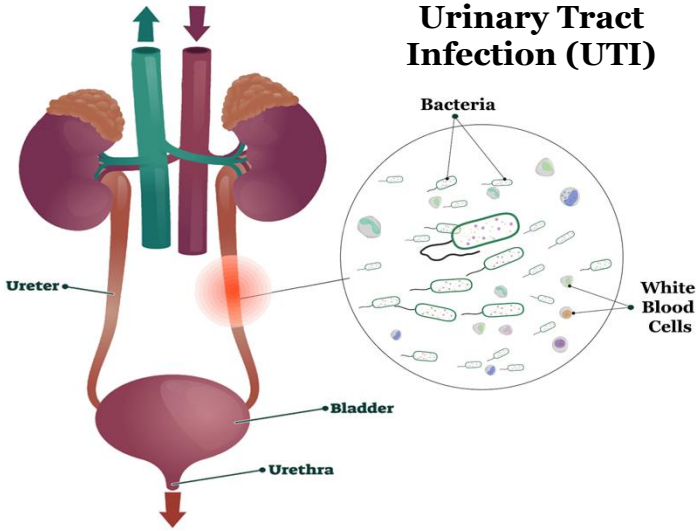
CATHERIZATION & ALTERNATIVE TREATMENTS

Intermittent Urinary Catheterization

If an individual has a form of bladder dysfunction making it difficult to void on their own, urologists may recommend at-home intermittent catheterization (every 3-5 hours typically) to empty the bladder prior to reaching dangerous pressures, prevent reflux of urine into the ureters and kidneys, and minimize pressure in the kidneys. With a little training from the urology team and good infection prevention practices, it's a manageable procedure for parents, caregivers, or the individual once old enough to self-manage. Catheterization is often used in conjunction with medication to help relax the bladder and improve its ability to safely store urine.

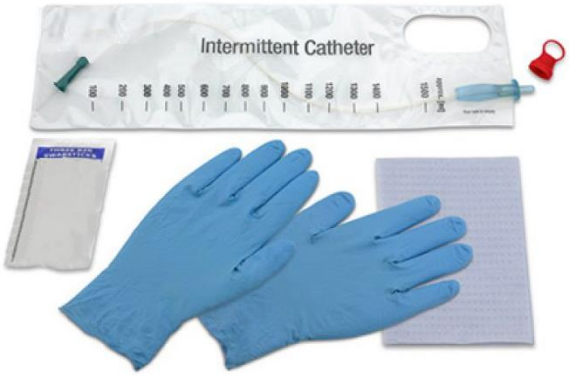
Medications

Antibiotics (such as Nitrofurantoin), bladder muscle relaxants (Oxybutynin, trade name Ditropan) may be prescribed by urologists if there's a history of UTIs to prevent additional infection, and of neurogenic bladder dysfunction.



Cutaneous Vesicostomy

An operation that makes an opening from the bladder to the abdomen just below the belly button. The opening (stoma) lets urine drain out of the bladder continuously.



Appendicovesicostomy

Also known as the Mitranoff Procedure, it surgically redirects the bladder to a stoma opening in the belly button and individuals catheterize through the belly button. This also allows drainage of the bladder like a vesicostomy does but allows for continence and intermittent drainage rather than continuous. It is best for those who are able to catheterize themselves. [23]

UROLOGICAL HEALTH

While there may be various (and often perplexing) underlying causes to neurogenic bladder dysfunction, incontinence, urinary and/or kidney infection, the goal remains the same – **to preserve the function and health of the kidneys in order to prevent permanent kidney damage,** which can lead to loss of function and end-stage renal disease if not detected and treated early and consistently by urologists and nephrologists.

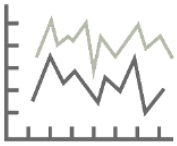
If renal/bladder function is normal (or stabilized after consistent management to treat any renal/ bladder conditions), urologists may recommend that those with a HADDS diagnosis have a renal/bladder ultrasound at least annually (if not more regularly) to check for bladder distention and dilation (hydronephrosis) in the kidneys, as well as to look at the general appearance of the kidneys.

Dr. Irina Stanasel, a Pediatric Urologist and Assistant Professor in the Department of Urology at UT Southwestern Medical School, has treated many children living with HADDS in North Texas. Dr. Stanasel understands the challenges of treating a rare disease and is committed to making herself available via email to fellow Urologist to discuss HADDS, how it displays and the best approach to managing care.

To connect, email irina.stanasel@utsouthwestern.edu

GASTROENTEROLOGY TESTING & TREATMENT

GASTROENTEROLOGY TESTING & TREATMENT



- **Evaluation:** Initial evaluation by a gastroenterologist is recommended for those living with HADDS, and regular evaluations thereafter if an individual is having chronic acid reflux, failure to thrive, difficulty eating/ swallowing, constipation or hypotonia related motility issues associated with HADDS.

- **Acid reflux, Difficulty eating:** Providers may prescribe different medications (Prevacid), dietary changes, or even a referral to a nutritionist/dietician if having difficulty with acid reflux and eating. For those with swallow dysfunction, using Thick-it, a food & beverage thickener, is recommended.
- **Failure to thrive:** Providers may prescribe a high-calorie supplemental formula (Pediasure Peptide 1.5, etc.), recommend regular visits to track height/weight progression, and/or referral to nutritionist if having difficulty gaining weight.

- **Constipation:** Providers may recommend (or even prescribe) medications to treat constipation such as milk of magnesia or miralax, among other options.

- **Gastrostomy tube (g-tube):** Has been indicated for some children with severe swallowing, breathing issues, laryngomalacia or reflux
- **Oropharyngeal dysphagia (swallowing issues):** Providers may recommend a swallow study, endoscopy, possibly Botox injections and exercises.

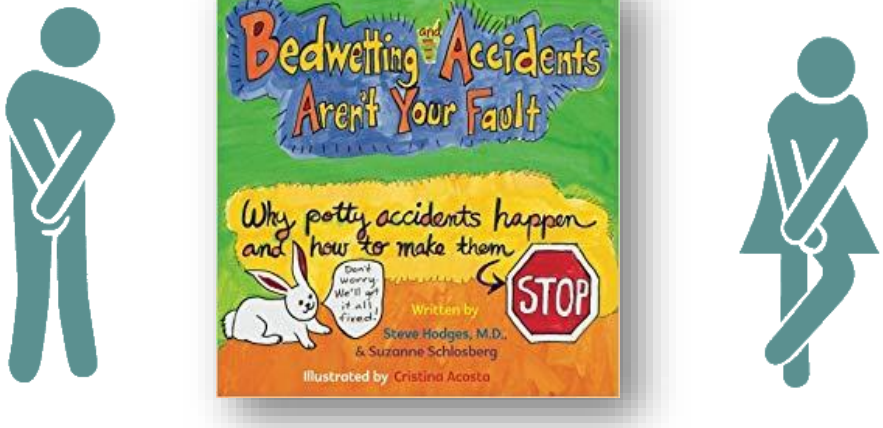
- **Aspiration treatment:** A supraglottoplasty surgery may be recommended by providers in some cases, in order to alter malformed structures of the upper larynx, which helps with laryngomalacia to breathe easier and may help reduce aspiration.

GASTROENTEROLOGY TESTING & TREATMENT

- **Fecal incontinence can lead to severe urology issues:** Fecal incontinence occurs when individuals voluntarily or involuntarily hold the bowel in the rectum. This can push up against the bladder and cause urinary incontinence by reducing the sensation of needing to void the bladder. This can lead to an increased risk of bladder distention, reflux and swelling of the ureters and kidneys, eventually causing a UTI and/or kidney infection. Thus, close multi-disciplinary coordination between gastroenterologists, urologist and nephrologists is needed to determine proper diagnosis and treatment of incontinence (fecal and urinary).

- **Stool consistency:** In children, normal stools should come out with a soft oatmeal/soft-serve ice cream/apple sauce consistency. If a harder consistency than that, it may be an indication of constipation, which indicates an evaluation with a child's pediatrician and/or gastroenterologist is indicated.

- **Tips for managing constipation:**
  - Sitting on the toilet daily after meals
  - Using a step stool
  - Squatty potty use
  - Good fluid intake throughout the day
  - Stool softeners
  - Laxatives – osmotic or stimulant
  - Suppositories / enemas
  - Miralax, Milk of Magnesia, Prunes



Note: Consult your physician first regarding gastroenterology issues

- Check out the book It's No Accident by Dr. Steve Hodges, a Pediatric Urologist at Wake Forest University School of Medicine. They're great resources for the management of constipation, wetting and other urinary issues. [24]

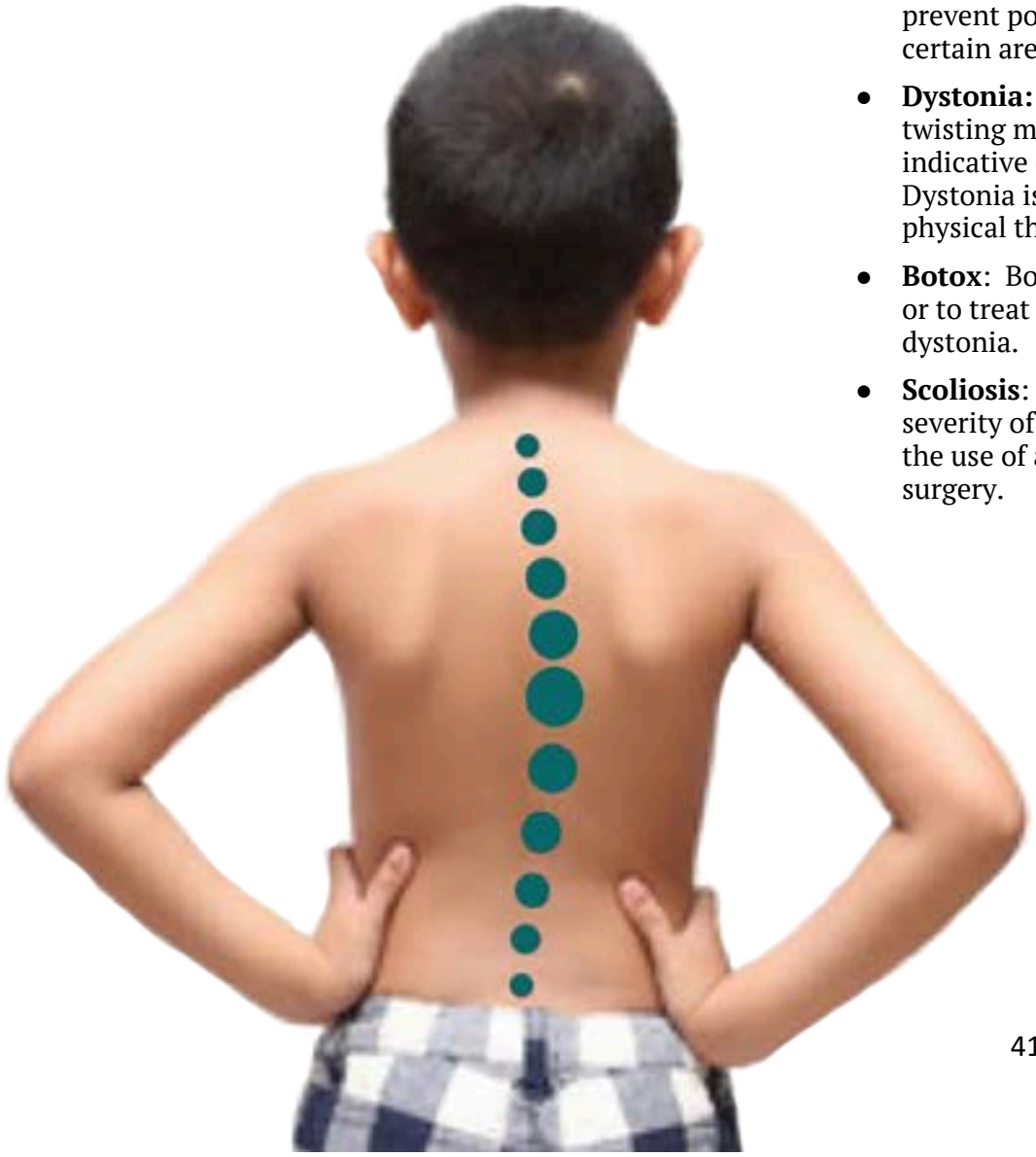
OPHTHALMOLOGY TESTING & TREATMENT

OPHTHALMOLOGY TESTING & TREATMENT

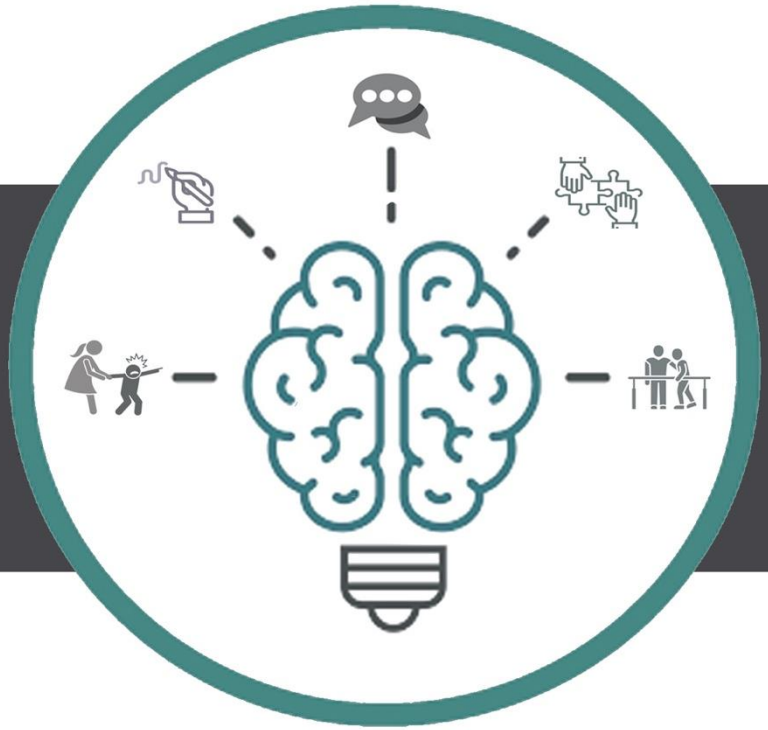
- It is normal for a newborn's eyes to wander or cross occasionally during the first few months of life. But once an infant is 4 to 6 months old, the eyes usually straighten out. If one or both eyes continue to wander in, out, up, or down — even once in a while — it's probably due to strabismus and a referral to a pediatric ophthalmologist is indicated. Early diagnosis and treatment, preferably before age 2, improve a young child's chances of having straight eyes and developing good vision and depth perception.

- Treatment for strabismus may include eyeglasses or eye patching as first-line treatment options. If unsuccessful, providers may prescribe atropine eye drops or eye muscle surgery. Many children with HADDS have had successful eye surgeries to correct crossed eyes, although needing multiple eye surgeries over time to correct strabismus isn't uncommon.

MUSCULOSKELETAL TESTING & TREATMENT



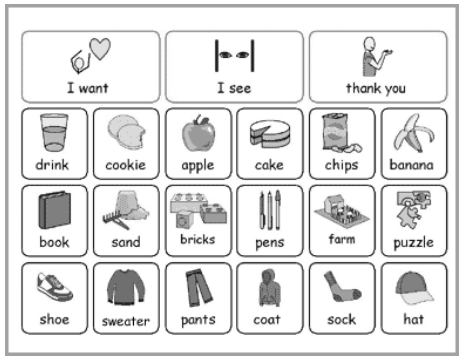
- **Torticollis:** Often treated with physical therapy and wearing a helmet (to prevent positional plagiocephaly, resulting from a flat spot that can develop in a certain area on a baby's head if their head is turned to the side for long periods).
- **Dystonia:** Involuntary muscle contractions that can cause slow, repetitive, twisting movements or abnormal postures. However, these movements are not indicative of a seizure. An EEG/MRI may be ordered to rule out seizures. Dystonia is often caused by fatigue. Treatments may include medication and physical therapy.
- **Botox**: Botox injections to treat clubbed foot (in calf muscles, achilles tendon), or to treat tight, hypertonic muscles (in hip flexors, hamstrings) or in cases of dystonia.
- **Scoliosis**: There are three main treatment options depending on the type and severity of scoliosis -- it may be monitored by healthcare providers, treated with the use of a thoracolumbrosacral orthosis (TLSO back brace), or corrected with surgery.



TYPES OF THERAPIES

FIRST LINE THERAPIES

First-line therapies for HADDS include Speech, Physical, Occupational and ABA therapy. They've helped hundreds of individuals living with HADDS progress in various areas. The key is to start these interventions early and consistently and to engage in therapy sessions so lessons learned can be applied by parents/caregivers at home regularly outside of therapy time. Additionally, it's valuable to have speech, physical, occupational or ABA therapists in the private setting coordinate by phone/email/in person with their counterparts and teachers in the school environment consistently to ensure therapy efforts are being channeled in the same direction.



Speech Therapy (ST): Early and consistent ST in the first 5-10 years of life (or longer) has proven beneficial to many with HADDS. For nonverbal toddlers with HADDS the focus should be on enabling communication first, even if through signing and adjunctive use of an Augmentative Alternative Communication (AAC) Device. The second priority should be on developing verbal speech. Create a ST treatment plan based on your loved one's unique current abilities and needs -- not on a blanket diagnosis. Parents have recommended a variety of excellent ideas for improving non-verbal and verbal communication:

- **Sign language:** Early introduction of signing skills has provided a valuable method in which to communicate until verbal speech follows for many.
- **AAC Devices / Apps:** Provide nonverbal communication support. Recommended programs include - ProLoQuo2go, Touchchat HD (for Ipad), LAMP, Accent 1000 communication device, Wego 10, Go Talk Now Plus, and Let Me Talk, among others.
- **PECS (Picture Exchange Communication System):** Using pictures in combination with words to communicate, make choices, show a daily task schedule, etc.
- **Kaufman cards:** Effective tool for helping them sound out certain words, syllables to become more vocal.
- **Mouth exercises**
- **Recorder Microphone:** Using a children's recorder toy with a microphone can motivate a child to verbalize more often
- **Feeding therapy:** SLPs can also help provide feeding therapy, which is important for HADDS children with chewing and swallowing difficulties early in life.
- **More than Words:** A communication program that includes a book, DVD series and classroom training (optional) with great ideas on how to communicate in various ways with children (or individuals) with disability. This program is recommended by some SLPs: hanen.org/Programs/For-Parents/More-Than-Words.aspx
- **I Want to Tell You Books:** Soundboard books that offer multiple communication approaches, between photographs, soundboard audio, and sign language - iwanttotellyoubooks.com/

FIRST LINE THERAPIES

Physical Therapy (PT): Early and consistent PT throughout childhood (and in adolescent and adult years for some) has proven very beneficial to many living with HADDS overcome hypotonia and ataxia related difficulty with standing, walking and going up and down stairs. It's recommended that children continue PT regularly throughout childhood, as for some as they reach puberty, their muscles become ***hypertonic*** (tighten), making it difficult to walk or even standup anymore. Maintaining regular PT may help prevent or manage symptoms associated with hypertonia for some. General recommendations from families living with HADDS that have aided in PT and improved their child's mobility include:

- **Strollers / Standing devices / Mobility devices:** Special needs stroller, Convaid adaptive stroller, EasyStand's Sit-to-Stand standing frame, mobile stander, wooden wagon (a toddler push wagon/walker) to provide independence and stability, Forward/ Traditional Walker, Posterior Pediatric Walker (Drive Nimbo), Gait Trainer (Mini Grillo), and Smart Drive Power Assist Wheelchair

- **At-home pediatric treadmill:** Great for toddlers and children to develop coordination, strength and balance with walking. Combine it with a TV or music to help keep children focused and motivated to continue walking.

- **Protective padding:** Foam letter mats on floors to buffer falls in playrooms, padding corners, upholstered ottomans, etc. HADDS children are prone to losing their balance and falling, leading to frequent bruises, cuts and even broken bones.

- **Orthotics:** Such as SMO, AFO orthotics for hypotonia / pronation. Consult with physical therapist and pediatrician to see if a referral for orthotics would be beneficial). Once fitted with an orthotic to wear over socks, buy a shoes size that's wide and a size bigger than the child usually wears so it can fit over the orthotic properly. Check out Billyfootwear.com, which offers stylish shoes that zip open/closed, allowing for easier wear over braces/orthotics.

- **Bikes:** Strider bike to develop balance, Junior stabilizer wheel kit training wheels, Amtryke (ambus.org), Rifton pediatric adaptive tricyles (Medicaid may pay for), Wheelchair Bike

FIRST LINE THERAPIES

Occupational Therapy (OT): In addition to speech and physical therapy, many children living with HADDS receive occupational therapy beginning early in life. OT is a treatment that works to improve fine and gross motor skills and motor planning. It can also help kids who struggle with self-regulation and sensory processing. The therapy is tailored to a child's specific needs. Before it begins, an occupational therapist looks at a child's strengths and challenges, and the tasks that child has trouble with. The therapist will then create a program of activities for the child to work on. OT consists of exercises and activities to build specific skills that are weak. For example, if a child has very messy handwriting, therapy may include multisensory techniques to help with handwriting. If a child struggles with focus, the therapist might have that child do full-body exercises before sitting down to do homework. The earlier a child starts OT, the more effective it tends to be. Being able to do basic tasks can also help build up kids' self-esteem and confidence, which can drop when they are struggling, especially in front of their peers.[25] Learn more at understood.org.

- **OT Tip:** Many children with HADDS suffer from intention tremors and motor coordination difficulties. Liftware.com offers stabilizing, self-leveling spoon handles, which are excellent for younger children learning to eat with utensils.

Applied Behavior Analysis (ABA) Therapy: ABA therapy has proven quite beneficial for individuals with HADDS, many of whom display autistic tendencies. It's the front-line therapy for those with autism and autistic tendencies and focuses on improving specific behaviors, such as social skills, communication, reading, academics and adaptive learning skills, such as fine motor dexterity, hygiene, grooming, domestic capabilities, punctuality, and job competence. ABA is typically offered in home or in day care outside of the school setting, and for longer sessions (2-5 hours per day) for 4-5 days per week. It combines and reinforces much of what's taught during speech, physical and occupational therapy into everyday activities while in an individual's normal living environment. To learn more about how ABA is helping those with HADDS, check out the HADDS blog post interview with ABA provider Traci Ramos: Hadds.org/post/aba-therapy-hadds.

ADDITIONAL THERAPIES

There are many other excellent therapy options that HADDS parents and caregivers report have helped their children make great strides physically, verbally, and behaviorally! The key is to find one or more therapy activities that keep them motivated.

Music therapy: Many parents and caregivers have found that music therapy, as a supplement to consistent speech therapy, has motivated their children to engage, verbalize more often, and achieve other self-care and academic goals.

Aquatic Therapy: A physical therapy approach that is especially helpful for some children as they reach puberty, when for some, muscles and joints get overly tight (hypertonia), making walking difficult.

Hippo therapy: While riding a horse, physical therapists, occupational therapists, and speech/language pathologists apply the movement, rhythm, and repetition of the horse as a treatment strategy to help patients achieve therapeutic goals.

Therapeutic horseback riding: Riding horses to help improve core strength, self-esteem, increase facial expressions, provide emotional support, learn a skill, follow directions, and achieve other goals.

Dance/ ballet: Beneficial to improve balance, muscle strength and memory, coordination and socialization.

Animal-assisted therapy: Motivating individuals through engagement with animals. The goal is to improve an individual's social, emotional, or cognitive functioning. One example is the non-profit Hand in Paw - https://handinpaw.org/

Sports therapy: The Special Olympics (specialolympics.org), Baseball (Miracle League Ball – miracleleague.com), Ice sled hockey, hand-cycling, etc...have helped with strength, coordination, socialization, modeling behavior, and improve the self-confidence of children, teens and adults with HADDS.

Social skills class: Some living with HADDS can struggle with what's socially acceptable behavior and socialization. Social skills classes are geared towards older children, teenagers and adults to work on social communication skills, eye contact during communication and understand and respond to social cues.

Oh, the Places You'll Go - Rare Disease Edition

Today is your day to breathe very deep. This is not a nightmare. You are not asleep.
Oh, the places you'll go, now that you're aware, there's travel involved when conditions are rare.
To a specialist doctor who is far away, but might have some answers, you'll travel one day. The process of intake will tax your poor brain, as you try to give details again and again.

Oh, the terms you will learn, as you go to and fro, from office to office of doctors who know.
And the things that you'll see when you go to PT, like braces and crutches and more in OT.
You'll see rods and wires and wheelchairs, too, and strange looking things that must be new.

Oh, the things that can happen, and frequently do, when you mix up the terms that are so new to you.
But those medical terms that were so hard to say, when you started out here, will be easy someday.

Oh, the way that you'll feel once you find the others, who share your condition like sisters and brothers
You'll be part of a group with whom you can share, you'll know that, though rare, you needn't despair.
You will get together with similar folk, who'll help you raise funds to give you some hope
While you're looking for answers here and there, Hospitals, medical centers and just everywhere.

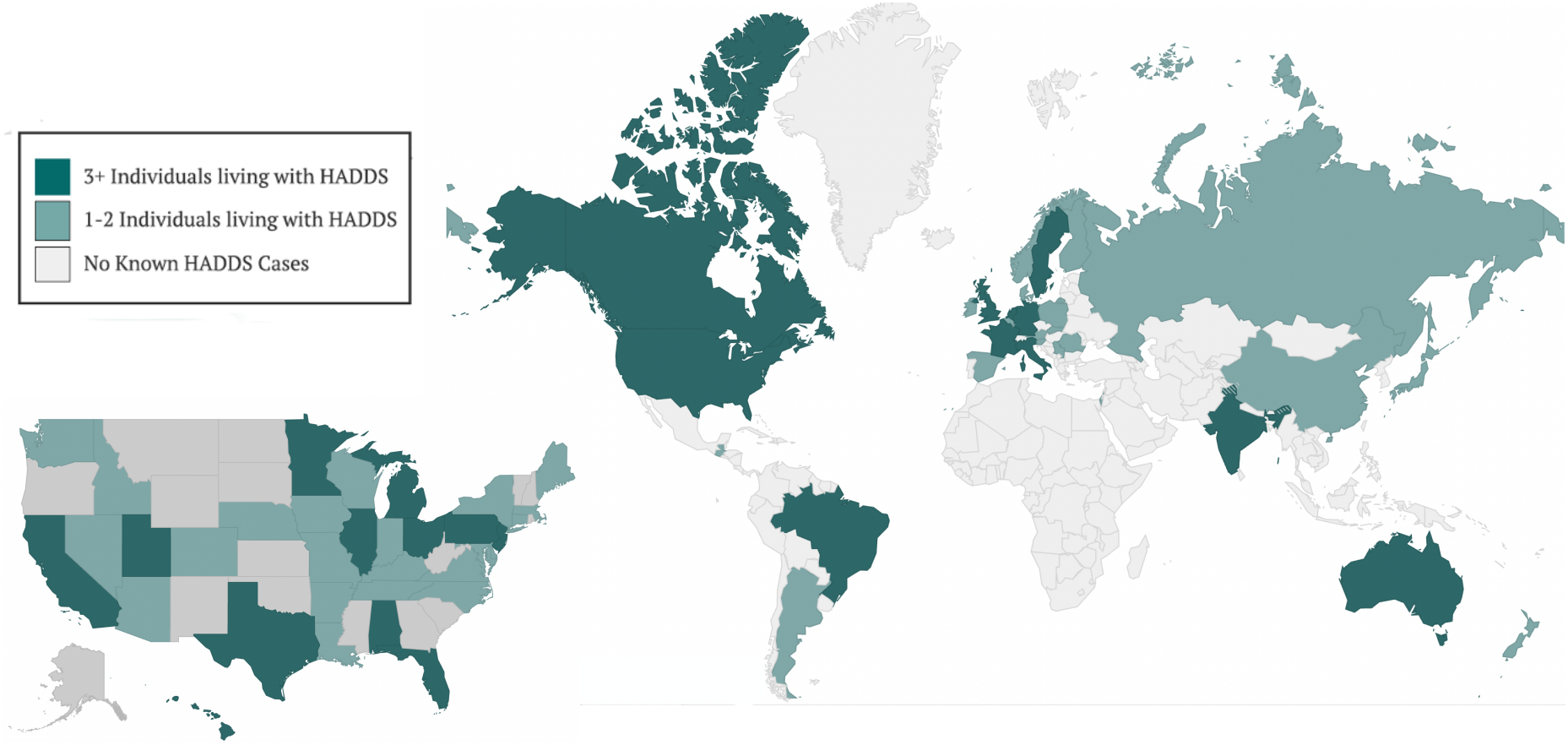
Yes, acceptance is hard as you learn how to deal, and reach out to others who know how you feel There are times you will cry and wish it weren't so, but you'll learn to be strong in those places you'll go.

~Denise Crompton, Rare Disease Parent

V. Community Map

The Global Prevalence of HADDS

Approximately **200 individuals** (mostly children) globally have been diagnosed with HADDS in the past 5+ years since it was originally discovered. Of those, the vast majority reside in the U.S. or Europe. It's estimated that there may be upwards of several thousand with the condition worldwide who simply have not received a diagnosis yet due to lack of access to care, the high cost of genetic testing, or because many are likely now adults and simply are not aware of the newly discovered genetic cause behind their lifelong condition.



CONNECT WITH THE GROWING HADDS FAMILY

The HADDS community has grown exponentially since its discovery in 2016! It is a globally engaged community where members offer encouragement and learn from each other through public and private Facebook groups, email, phone calls and Zoom Social Circles. In addition, many actively fundraise to support research and each other, attend the HADDS Conference and/or Social Clinic Weekends annually in Houston, TX and host regional meetups with other HADDS families.

EBF3 HADDS Foundation: HADDS.org / Facebook / LinkedIn / Instagram

Established in 2019, the Foundation leads fundraising efforts for research and community support, offers resource packets, links to publications & media reports, coordinates HADDS conference and social clinic events, leads awareness campaigns, offers merchandise in the HADDS Shop to promote awareness and pride in our growing community.

Facebook EBF3 – HADDS (EBF3 genetic mutation) private group:

A private group with 200+ HADDS individuals and parents or primary caregivers of those affected by HADDS. The purpose of the group is to share support and resources. It's a place to make new HADDS friends, share in each other's milestones and setbacks, encourage and learn from each other.

Facebook EBF3 – HADDS Public Forum

A public group with 251+ members, it's a great site to gather information, find resources, and ask question about HADDS. It's a place to connect with others who have a loved one, a friend, a student, or a therapy client with HADDS.

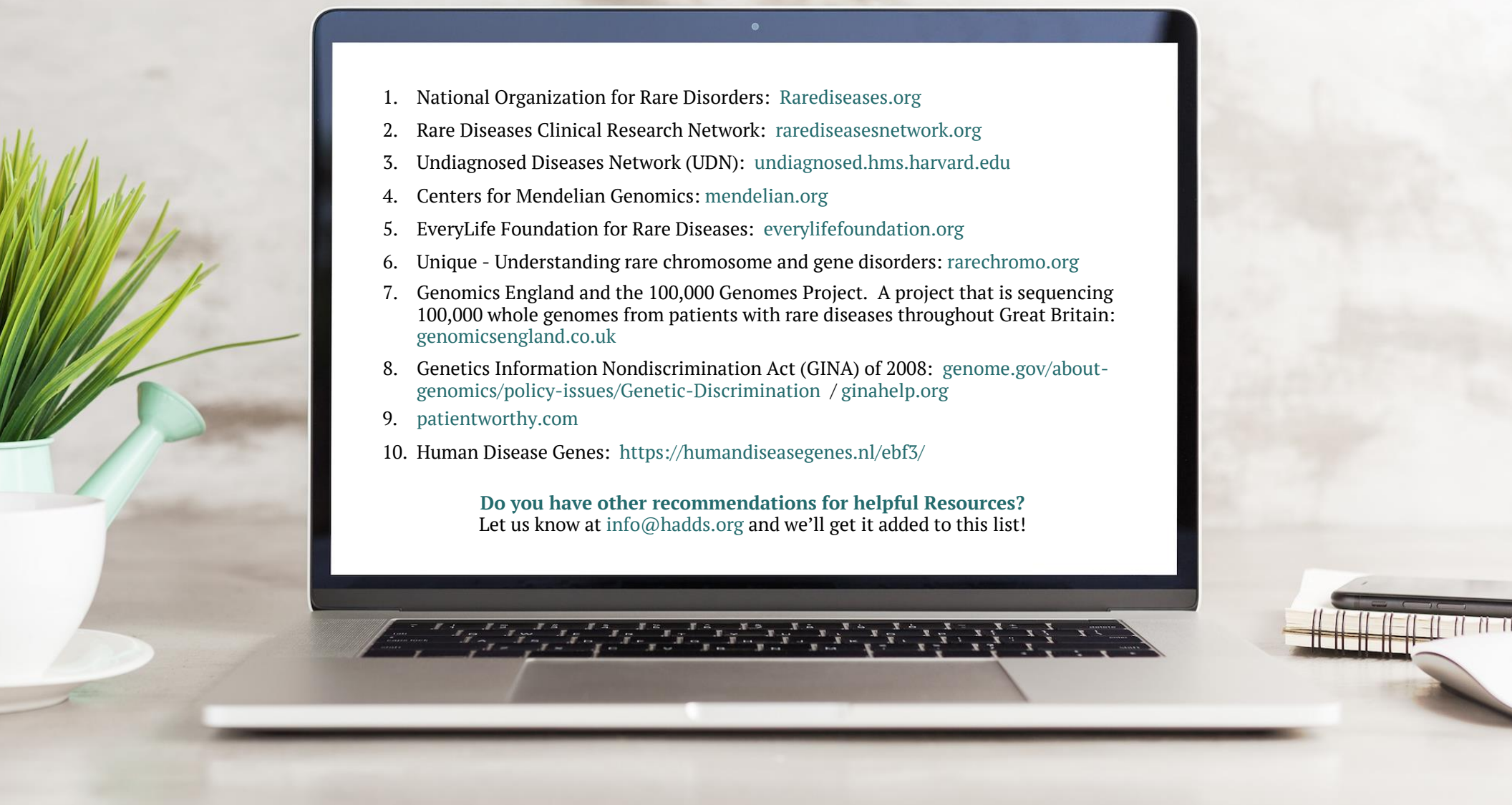
EBF3-HADDS Families Blog:

Ebf3blog.wordpress.com by Kelly Mastin, a mother from Texas, USA whose teenage daughter is living with HADDS

https://www.handlinghadds.com/ by T'Mia Raynor, a mother in Washington, DC, discusses life with a child living with HADDS

Empowering Different, facebook.com/HADDSlove by Jessy Safar, a mother in Ottawa, Canada, whose daughter is living with HADDS

HADDS GENETICS RESOURCES



1. National Organization for Rare Disorders: Rarediseases.org
2. Rare Diseases Clinical Research Network: rarediseasesnetwork.org
3. Undiagnosed Diseases Network (UDN): undiagnosed.hms.harvard.edu
4. Centers for Mendelian Genomics: mendelian.org
5. EveryLife Foundation for Rare Diseases: everylifefoundation.org
6. Unique - Understanding rare chromosome and gene disorders: rarechromo.org
7. Genomics England and the 100,000 Genomes Project. A project that is sequencing 100,000 whole genomes from patients with rare diseases throughout Great Britain: genomicsengland.co.uk
8. Genetics Information Nondiscrimination Act (GINA) of 2008: genome.gov/about-genomics/policy-issues/Genetic-Discrimination / ginahelp.org
9. patientworthy.com
10. Human Disease Genes: https://humandiseasegenes.nl/ebf3/

Do you have other recommendations for helpful Resources?
Let us know at info@hadds.org and we'll get it added to this list!

NORD National Organization for Rare Disorders · RARE DISEASES CLINICAL RESEARCH NETWORK · AGTC · Unique · EVERYLIFE FOUNDATION FOR RARE DISEASES 10 YEARS OF ADVOCACY · UDN Undiagnosed Diseases Network · Genomics england

HADDS RESOURCES

Family Support Resources:

Facebook – Chromosome 10 Disorder group: facebook.com/groups/chromosome10disorder

Facebook – Hypotonia Parent Support group: facebook.com/groups/HypotoniaParentSupportGroup/?ref=share

Global Genes – Allies in Rare Diseases: https://globalgenes.org/ / Parenting a Child with a Life Limiting Illness: https://globalgenes.org/wp-content/uploads/2014/02/GG_toolkit_4final_print.pdf

Understood – Site with resources for families of children with learning disabilities, ADHD: understood.org

American Speech-Language-Hearing Association: asha.org

Autism Speaks – helpful resources for HADDS individuals with autistic tendencies: autismspeaks.org

Gallaudet University – American Sign Language (ASL) online courses (free): gallaudet.edu/asl-connect/asl-for-free

Cromwell Center for Disabilities Awareness: cromwellcenter.org

Early Childhood Intervention contact info by state: https://www.cdc.gov/ncbddd/actearly/parents/state-text.html / https://www.autismspeaks.org/state-early-intervention-information

Age 0-5 Early childhood Development - CDC: cdc.gov/ncbddd/actearly/index.html

Department of Health and Human Services (DHHS) – Programs for people with disabilities: https://www.hhs.gov/programs/social-services/programs-for-people-with-disabilities/index.html

Do you have other recommendations for helpful Resources?

Let us know at **info@hadds.org** and we'll get it added to this list for other families!

HADDS RESOURCES

Family Support Resources:

Children's Miracle Network: childrensmiraclenetworkhospitals.org

Make-A-Wish Foundation: wish.org

Morgan's Wonderland & Islands of Adventure – The world's first ultra-accessible theme park and splash park geared towards children living with disabilities, located in San Antonio, TX: morganswonderland.com

Go Baby Go – A program that provides modified, ride-on cars to young children with disabilities so they can move around independently. At least two families with HADDS have already benefited from this wonderful program offered at their local universities: https://www.yourcpf.org/cpproduct/go-baby-go-the-ultimate-toy-hack/

Tiny Superheroes - Nominate a child with HADDS to receive a custom-made cape, because what they and their families are doing to overcome barriers each day is heroic! tinysuperheroes.com

More Than Words – A communication program that includes a book, DVD series and classroom training (optional) with great ideas on how to communicate in various ways with special needs children, this program is recommended by some SLPs: hanen.org/Programs/For-Parents/More-Than-Words.aspx

Bed Wetting and Accidents website and books – Developed by Dr. Steve Hodges, a Pediatric Urologist at Wake Forest University School of Medicine, it offers great resources on the management of constipation, wetting and other urinary issues: bedwettingandaccidents.com

Easterseals – A nonprofit that assists people with physical and mental disabilities, and special needs. Parents can find support for a child who has a diagnosis at birth and there are services for people who have a disability due to disease, injury, or aging. Professionals at Easterseals help people overcome barriers, achieve independence, and reach their goals: Easterseals.com

Do you have other recommendations for helpful Resources?

Let us know at **info@hadds.org** and we'll get it added to this list for other families!

HADDS IN THE NEWS

2022

Finding the right diagnosis for one child can help millions more, Texas Children's Hospital/Jan and Dan Duncan Neurological Research Institute - Houston, TX - 5/16/2022 https://nri.texaschildrens.org/news/healing-one-child-can-help-millions-more

Inclusive School: There is still effort to be made Top Sante, Issue 379: April 2022 Edition - Montrouge, France - 3/1/2022
https://www.hadds.org/_files/ugd/badd80_d59ccbf28ebd441fa6875642d1be277f.pdf (Translated with original article included)

February is HADDS Awareness Month: Local family raises awareness about HADDS - Bancroft, Ontario Canada - 2/25/2022
https://en.calameo.com/read/003289257feab6f6d8057?fbclid=IwAR0WRiaxqe7nJkWwxnmNT6BYtHXVEkHc6QgMWKAzDMSa6LgE4rGs2MmnkqY

2021

The EBF3 HADDS Foundation Publishes the Understand HADDS Education Packet - Houston, TX - 2/23/2021
https://www.hadds.org/hadds-resources

The EBF3 HADDS Foundation Gifts $25,000 for HADDS Research - Houston, TX - 7/23/2021
https://www.hadds.org/foundationgiftsnriresearchmoney

À Mailly-Maillet, la chienne Noisette a changé la vie de Maxime, 7 ans, touché par une maladie génétique
(Translated Title: In Mailly-Maillet, the dog Noisette changed Maxime's life, 7 years old, affected by a genetic disease)
Courrier Picard, Amiens, France - 2/9/2021
https://www.hadds.org/_files/ugd/badd80_0aafe192f1244bf5a803a34ca8745d4e.pdf
Translated side-by-side article with original reference link

HADDS IN THE NEWS

2020

EBF3 HADDS Foundation hosts first HADDS In Motion Global Fun Run, raising $20,000! – 11/2/2020

The Foundation Collaborates to Publish the First HADDS Book -- Abled: Same But Different
EBF3 HADDS Foundation, Houston, TX - 8/13/2020
https://www.hadds.org/abled-same-but-different

Dr. Chao awarded Philip R. Dodge Young Investigator Award, Baylor College of Medicine, Houston, TX - 6/30/ 2020
https://www.bcm.edu/news/chao-awarded-philip-r-dodge-young-investigator-award?fbclid=IwAR1zqp55akRnD4mXy6kuLJOBmUcWMVoSWfSxT7iX-4mQO8iSc21OqjVV6Ng

The EBF3 HADDS Foundation Turns One and Celebrates Growing Community with HADDS Awareness Month in February - EBF3 HADDS Foundation, Houston, TX - 1/26/2020
https://www.hadds.org/foundation-turns-one

2019

A brother's love: Researching for a cure - Texas A&M University - 9/24/2019
https://engineering.tamu.edu/news/2019/09/a-brothers-love-researching-for-a-cure.html

Texas Children's hosts inaugural family conference for EBF3-HADD syndrome – TCH / NRI - 8/26/2019
https://nri.texaschildrens.org/news/texas-children%E2%80%99s-hosts-inaugural-family-conference-ebf3-hadd-syndrome

Hazlet sixth-graders design motorized mini-car for 2-year-old with special needs - USA Today - App. - 4/16/2019
https://www.app.com/story/news/local/values/2019/04/16/hazlet-6th-graders-design-mini-car-2-year-old-special-needs/3436892002/

Dr. Hsiao-Tuan Chao named new McNair Scholar - Baylor College of Medicine - 3/13/2019
https://www.bcm.edu/news/awards-honors-faculty-staff/dr-hsiao-tuan-chao-named-new-mcnair-scholar

The EBF3-HADDS Foundation becomes an official 501c3 Non-Profit! – 2/20/2019

Easter seals is making a difference for kids and their families - Eye-9 News, Washington, DC - 2/6/2019

https://www.wusa9.com/video/entertainment/television/programs/great-day-washington/easterseals-is-making-a-difference-for-kids-and-their-families/65-2d3d057c-abf2-4d99-904c-9e402bf1f251?fbclid=IwAR15zKTW6iRrOKo1Wy4IWL0L355nbITUFEKNvhjo72HGvQKe-WZuHQRAbjA

About the EBF3 HADDS Foundation

The EBF3 HADDS Foundation was founded in February 2019 with hopes of connecting families and building a centralized information center for research, community events, resources and support. To learn more about our work, visit **HADDS.org.**

Mission

To enhance the lives of people with HADDS through research, education, support and advocacy.

Vision

Raise educational awareness and funding for research so that every person with HADDS:

- Has a supportive community
- Is able to reach their full potential
- Has access to the most current educational/therapy materials
- Has access to the most current research

The Foundation is a 501c3 Registered in the U.S., EIN: 83-2757964

Values

Ethical & Transparent: It is the Foundation's priority to be ethically and financially responsible when advancing our mission in the areas of research, education, support and advocacy.

Committed: We are nothing as an organization if we are not committing our energy, talents and resources consistently towards research and education. Commitment drives progress!

Inclusive & Collaborative: Be ambassadors for inclusion, welcoming and facilitating an environment of hope, belonging and community for all impacted by HADDS globally.

Community Engagement

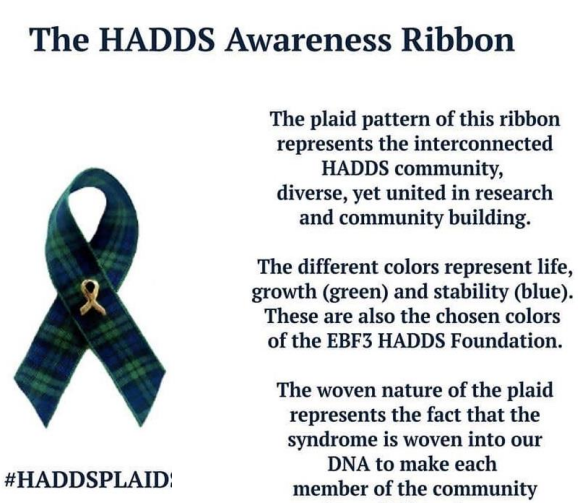
HADDS Plaid Awareness Campaign

Small communities like ours have to make a concerted effort to educate our local communities about HADDS in hopes of promoting understanding and inclusion. One of the easiest, most recognizable ways to jumpstart sharing is by adopting an awareness ribbon. Awareness ribbons are worn as a figurative information symbol or question mark, signaling to others that you have information or have been impacted by and/or passionate about a cause. In many cases, the ribbon is just enough to prompt a casual conversation about HADDS and generate awareness.

Similar to the Autism Society's puzzle awareness ribbon, we felt a patterned ribbon was appropriate given the rare nature of the syndrome; one singular color wouldn't appropriately represent our uniqueness or diverse community.

If you would like to participate in the campaign or have a fundraiser or event that supports HADDS, wear black watch plaid clothing and you can purchase the HADDS Plaids Awareness Ribbons in the Foundation's Shop. In addition to the awareness ribbons, there are other products for sale that can prompt additional opportunities for community education, so check those out as well!

Hadds.org/post/hadds-plaid-awareness-campaign

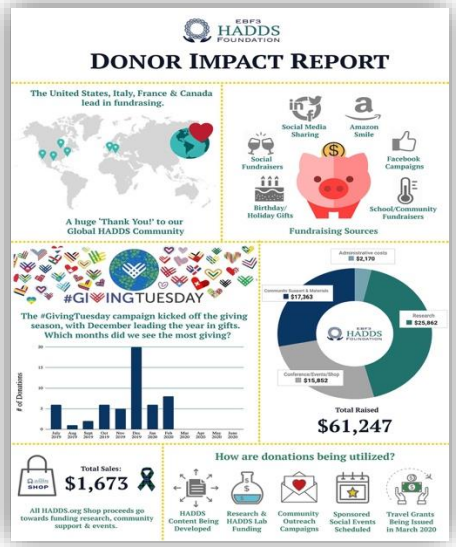


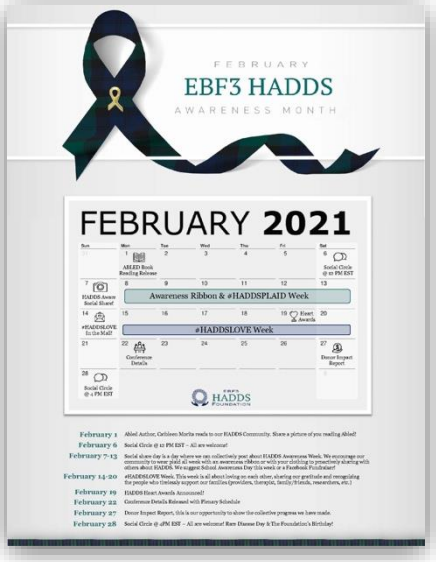
COMMUNITY ENGAGEMENT

HADDS Awareness Month – February

Our community LOVES February! It's the month of love, with Valentine's Day, Rare Disease Day (always falls on the last day of February), and the EBF3 HADDS Foundation was established in February of 2019. February is a time to celebrate our loved ones with HADDS, those who care for them and raise awareness. During the month each year, various events are held locally and via social media, including:

- HADDS School Awareness Day
- HADDS Creative Design Contests
- HADDS Valentine's Day mailing
- HADDS Plaid Awareness Ribbon Week
- #HADDSLOVE Family Challenge
- Conference/Social Clinic Details
- Awareness Themed Social Circle / Podcast
- Donor IMPACT Day – February 28/29th



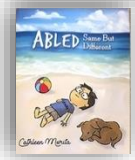


COMMUNITY ENGAGEMENT

HADDS School Awareness Day

Parents or caregivers are encouraged to work with their teachers and school administrators to develop a HADDS Awareness Day in February (or any day of the school year). It's a way to increase awareness, understanding and inclusion among peers. The Foundation has developed an info packet with ideas on the HADDS.org resource page: Hadds.org/hadds-resources

Do you have ideas for HADDS School Awareness Day? Email us at: info@hadds.org so we can add it to the info packet!)



Abled: Same But Different Book Reading
Visit: https://youtu.be/8BHFIYvbx8Q

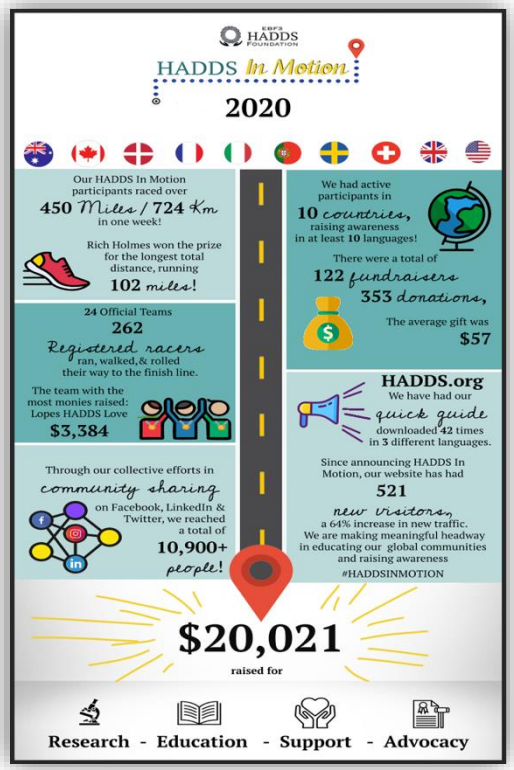
A HADDS Awareness School Event in Rome, Italy.

COMMUNITY ENGAGEMENT

EBF3 HADDS FOUNDATION

HADDS *In Motion*

The Virtual Fun Run is a global week-long event and fundraising challenge to raise awareness and support the individual(s) in your community with HADDS.



HADDS In Motion is one of the global community events scheduled every October.

Photos Top to Bottom:
Team Lopes Runners in Sydney, Australia, Team Slick in Chico, CA, USA and Team Mattia in Lake Como, Italy

COMMUNITY ENGAGEMENT

Fundraising Events

In a short time, our community has done an incredible job developing creative fundraisers to drive funding for research, conferences and supporting travel grants for HADDS families. Fundraising efforts have included:

- Giving Tuesday (the Tuesday following Thanksgiving)
- Donor IMPACT Day – on Rare Disease Day (Last day of February)
- Fundraising drives in honor of birthdays or other milestones (Facebook, GoFundMe, Birthday parties, etc.)
- Community or School fundraising events
- Dinners, Brunches or Auctions

Photos Top to Bottom:
#GivingTuesday is a global giving campaign, established to encourage people to do good in the world, giving of their voice, time or money.

Foundation Secretary, T'Mia Raynor and her husband Phillip, hosted a HADDS Brunch in Washington, DC in honor of her daughter Portland.

Anna Bergeron, a HADDS grandmother, is one of many who used their personal Facebook platform to raise money for her the Foundation on behalf of her granddaughter Coco.

Kaylani Sinclair made bracelets and sold them at a craft fair.

COMMUNITY ENGAGEMENT

EBF3 HADDS International Conference

Every other summer, the Foundation hosts the EBF3 HADDS International Conference at Texas Children's Hospital in Houston, TX. The inaugural conference was held July 25-27th, 2019 and was attended by over 100 members of our community, medical providers and researchers. Another 15 U.S. and international families engaged online during the live streamed video of conference lectures. To learn more about the first conference, check out: Hadds.org/inaugural-2019-ebf3-hadds-conferenc or the NRI article nri.texaschildrens.org/news/texas-children%E2%80%99s-hosts-inaugural-family-conference-ebf3-hadd-syndrome

EBF3 HADDS International Conference

COMMUNITY ENGAGEMENT

Social Clinic Weekend

Every other summer (the years when the International Conference is not being held) the Foundation hosts a Social Clinic Weekend at Texas Children's Hospital in Houston, TX. It's a casual 2–3-day event that's an opportunity for families that are in town to have initial or annual checkups with Drs. Chao & Wangler to meet up with other families and make new friends.

All families are welcome to register and attend the social gatherings, regardless of whether there is an official appointment at Texas Children's.

Events typically planned include:

- Pool & Pizza Party
- HADDS Lab Tour
- Houston Zoo or Children's Museum
- Parent discussion breakout sessions

REFERENCES

1. Sleven H, Welsh SJ, Yu J, et al. De Novo Mutations in EBF3 Cause a Neurodevelopmental Syndrome. Am J Hum Genet. 2017;100(1):138-150. doi:10.1016/j.ajhg.2016.11.020
2. Wangler M. What is HADDS? Non-Neurological and Genetic Findings. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
3. Chao, TH. The Neurological Impact of HADDS. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
4. Chao, TH. The Neurological Impact of HADDS. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
5. Stanasel, I. Potential Urological Implications of EBF3 Gene Mutation. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
6. Wangler M. What is HADDS? Non-Neurological and Genetic Findings. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
7. Wangler M. What is HADDS? Non-Neurological and Genetic Findings. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
8. Wangler M. What is HADDS? Non-Neurological and Genetic Findings. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
9. Chao, TH. Future Directions. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
10. Wangler M, Chao, TH. Discovery & Benefits of Rare Disease Research. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
11. Wangler M, Chao, TH. Discovery & Benefits of Rare Disease Research. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
12. Magoulas, PL. Genetics 101. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
13. Magoulas, PL. Genetics 101. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
14. Wangler, M. What is HADDS? Non-Neurological and Genetic Findings. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
15. Magoulas, PL. Genetics 101. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
16. Magoulas, PL. Genetics 101. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
17. Magoulas, PL. Genetics 101. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
18. Wangler, M. What is HADDS? Non-Neurological and Genetic Findings. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
19. Wangler, M. What is HADDS? Non-Neurological and Genetic Findings. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
20. Wangler, M. What is HADDS? Non-Neurological and Genetic Findings. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
21. Magoulas, PL. Genetics 101. Lecture presented at: Texas Children's Hospital; July 25, 2019; Houston, TX.
22. Stanasel, I. Potential Urological Implications of EBF3. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
23. Stanasel, I. Potential Urological Implications of EBF3. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
24. Stanasel, I. Potential Urological Implications of EBF3. Lecture presented at: Texas Children's Hospital; July 27, 2019; Houston, TX.
25. Wilmot, K. Occupational Therapy: What You Need to Know. Understood, 2020; accessed 25 January 2020: https://www.understood.org/en/learningthinking-differences/treatments-approaches/therapies/occupational-therapy-what-you-need-to-know

Our **HADDS** Story

Date of Diagnosis: _____

Variant: _____

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EBF3
HADDS
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