ARE YOU MISSING HUNTER SYNDROME?

Information for healthcare professionals

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Takeda

INTRODUCTION TO HUNTER SYNDROME

You may be one of the first physicians to recognise the signs and symptoms of Hunter syndrome.

A **rare combination** of common childhood complaints could indicate **Hunter syndrome, also known as mucopolysaccharidosis type II, (MPS II).**

Check the abdomen | **Check the ENT area** | **Check for other symptoms**

ACT EARLY*

Refer to a specialist today

This eBook provides information on the signs and symptoms of Hunter syndrome, including the importance of early referral, and the multidisciplinary management of the disease.

For more information, **visit huntersyndrome.info**

This eBook has been produced by Takeda for the use of **healthcare professionals located outside the USA**.

This resource is intended for an international audience outside of the USA and has been produced by Takeda. This resource has been developed in accordance with industry and legal standards to provide information for healthcare professionals about Hunter syndrome. Takeda makes every reasonable effort to include accurate and current information. However, the information provided in this eBook is not exhaustive.
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Basic information on Hunter syndrome, what it is and how it occurs

THE HUNTER SYNDROME COMMUNITY

Stories from families living with Hunter syndrome

SIGNS AND SYMPTOMS

Are you missing Hunter syndrome? Find out about the red flag cluster symptoms that may indicate the presence of Hunter syndrome

DIAGNOSIS

Read more on laboratory tests that can help to confirm a diagnosis of Hunter syndrome

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ABOUT HUNTER SYNDROME

What is Hunter syndrome?

Hunter syndrome, also known as mucopolysaccharidosis type II (MPS II), is a rare genetic disease almost exclusively affecting boys.[1] It is estimated that the condition is present in 1 in every 162,000 newborn babies.[2] Hunter syndrome can affect any part of the body and has a number of signs and symptoms.[3] In the majority of children these begin to show between the ages of 2 and 4 years.[4]

What causes Hunter syndrome?

Hunter syndrome is a genetic disease caused by the deficiency or absence of an enzyme called iduronate-2-sulfatase (I2S).[4]

In Hunter syndrome, the gene that codes for I2S contains a mutation (a change), which means that the enzyme is produced with errors that stop it working properly, or the enzyme is not produced at all.[5]

I2S is essential for breaking down particular molecules, known as glycosaminoglycans (GAGs).[4] If I2S is deficient or absent, as in Hunter syndrome, GAGs build up, which prevents cells from functioning properly.[4]

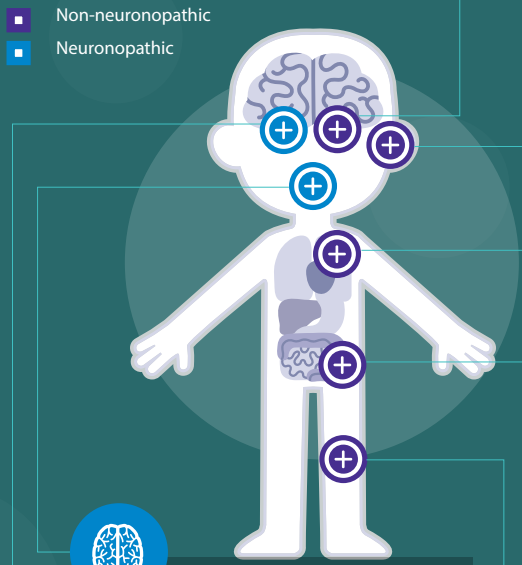
AIDEN AND AJ

Aiden suffered frequent **ear infections**. At the age of **18 months** old, around the time his brother, AJ, was born, he had his **adenoids removed**. At the age of 2, there was delay in Aiden's speech development, and he was referred for occupational therapy, physiotherapy and speech therapy. After a year, his paediatrician suggested that he see a geneticist. During the appointment the geneticist noticed that AJ had the same symptoms.

For more information, visit huntersyndrome.info/hcp

SIGNS AND SYMPTOMS

The range and severity of symptoms of Hunter syndrome is unique in each patient. However, the early symptoms overlap with common childhood complaints, making it challenging to detect and ultimately leading to diagnostic delays.[3] It is important to recognise the combination of red flag symptoms, such as: **otitis media, abdominal hernia, englarged adenoids/tonsils and enlarged liver/speen** that may indicate Hunter syndrome.[4]



HEAD

- **Distinctive** facial features [3]
- **Enlarged** tongue, tonsils, adenoids, epiglottis [3]
- **Irregular** or peg-shaped teeth [3]

EARS AND NOSE

- **Recurrent** infections [3]

BREATHING

- Upper airway **obstructions** [3]

ABDOMEN

- **Distended** abdomen due to enlarged liver and/or spleen [3]
- Bladder **obstruction** [3]

BONES AND JOINTS

- **Stiffened** joints and **claw-like** hands [3]

NERVOUS SYSTEM

- Difficulty chewing and swallowing [3]
- Motor skill impairment [3]
- Seizures [3]
- Carpal tunnel syndrome [3]
- Chronic diarrhoea [3]

DEVELOPMENTAL DELAY

Prevalence of symptoms from Hunter Outcome Survey analyses

There isn't a typical disease course in Hunter syndrome, however, there are common trends in the progression of the disease.

1-2 Years

Hernia [6]	**78%**
Otitis media [7]	**72%**

2-3 Years

Facial features [6]	**95%**
Enlarged liver/spleen [6]	**89%**
Any surgical procedure [8]	**84%**
Enlarged adenoids/tonsils [6]	**68%**
Any respiratory symptoms [9]	**70%**

3-4 Years

Skeletal sign/symptom [9]	**79%**
Hernia repair [8]	**50%**
Adenoidectomy [7]	**47%**
Behavioural problems [6]	**36%**
Enlarged tongue [6]	**70%**
T-tube insertion [7]	**50%**

4-6 Years

Hearing loss [7]	**67%**
Cardiac valve disease [10]	**63%**
Claw hand [9]	**53%**
Tonsillectomy [8]	**36%**

7-8 Years

Kyphosis/scoliosis [9]	**34%**
Carpal tunnel syndrome [9]	**27%**

HUNTER SYNDROME STORIES

AIDEN AND AJ

Aiden appeared to be a healthy baby boy when he was born. However, gradually though his first year of life, he began suffering from frequent ear infections. The family's paediatrician believed that these were 'typical' symptoms for a child at his age.

At age 18 months (around the time his brother, AJ, was born), Aiden had his adenoids removed. He was still cheerful, and enjoyed playing with his younger brother, but by the age of 2 years, Aiden's parents had noticed a delay in his speech development. Aiden was given occupational therapy, physiotherapy and speech therapy. By age 2 and half years, he wasn't improving and was referred to a geneticist.

The geneticist noticed several abnormalities with Aiden: the tips of his fingers were bent, the bridge of his nose was flat, and he was hairy. She additionally noticed than AJ had the same symptoms, and she suspected a genetic disorder in the family. Both brothers were soon diagnosed with Hunter syndrome.

Visit **huntersyndrome.info/hcp** to learn more about **Aiden and AJ**

SILAS

Silas was normal when he was born, but at around the age of 6 months, his parents noticed that the back of his head was becoming flat, and that he had difficulties holding his head up. He also didn't like being laid down upon his stomach. At age 1 year Silas fell ill with a severe cold, high temperature, and obstructive bronchitis. A doctor then investigated whether his head circumference had ever been recorded.

At age 2 years, Silas went for an MRI scan, which showed an abnormality. He was then referred for genetic testing, which confirmed a diagnosis of Hunter syndrome.

Silas is now exposed to illnesses from the other children at school, and he has problems interacting at kindergarten, due to his learning and speech difficulties. His parents also have to ensure that all doors are locked as he is prone to behaviour such as opening cabinets and potentially hurting himself.

Visit huntersyndrome.info/hcp to learn more about **Silas**

HUNTER AND KINGSTON

From the very beginning, Hunter was always sick. He was in the hospital or doctor's office every month with high fevers because of ear infections. He also had an umbilical hernia that never went away. When Hunter was 6 months old, his mother was pregnant with Kingston and by that time, Hunter was always sick.

To their mother, the two boys had always seemed normal, but Hunter had a big head and didn't start walking until he was 13 months old. He had ear infections, sickness, coughs, and colds. When Kingston was born, he was in intensive care for three weeks. He started off with lung problems and after that he was frequently on breathing treatments.

Hunter and Kingston are both cognitively affected and neither spoke until around the age of 4 years. They receive speech therapy and therapy for physical ailments and sensory issues, and attend a special needs school. Although Kingston is 6 years old, he only has 60 words and only usually uses 10 words a day.

Visit **huntersyndrome.info/hcp** to learn more about **Hunter and Kingston**

LIVING WITH HUNTER SYNDROME

SILAS

Although he attends kindergarten, Silas doesn't speak more than a few words. There is little interaction from him and all doors and cupboards must be locked to prevent him from injuring himself or his friends. These are the challenges we face every day.

Natalie, mother of Silas

HUNTER AND KINGSTON

Hunter and Kingston are both cognitively affected and neither spoke until around the age of 4 years. They receive speech therapy and therapy for physical ailments and sensory issues, and attend a special needs school. At the age of 6, Kingston has a vocabulary of 60 words and only uses 10 words a day.

Brittany, mother of Hunter and Kingston

If you suspect Hunter syndrome: REFER TO A SPECIALIST TODAY

DIAGNOSIS

Suspicion of Hunter syndrome usually follows the appearance of a range of red flag symptoms described earlier, particularly if they appear in clusters.[4] Physical examinations could then be done to assess non-neuronopathic symptoms of the disease, such as joint stiffness, enlarged abdomen, and the characteristic facial features of Hunter syndrome.[3] In older children, cardiac complications could also be investigated.[3]

AIDEN AND AJ

The geneticist noticed several abnormalities with Aiden: the tips of his fingers were bent, the bridge of his nose was flat, and he was hairy. She additionally noticed than AJ had the same symptoms, and she suspected a genetic disorder in the family.

Toni Ann, mother of Aiden and AJ

SILAS

"When he was 2, our little boy had an MRI scan. The consultant told us that the MRI showed an abnormality that might be a symptom of a rare disease called mucopolysaccharidosis.

A month later, blood test results confirmed that Silas had Hunter syndrome."

Natalie, mother of Silas

If you suspect Hunter syndrome: ACT EARLY, REFER TO A SPECIALIST TODAY

TESTING FOR HUNTER SYNDROME

Urinary tests

- Urinary tests may be the first diagnostic indicator of disease, however a negative result does not necessarily rule out the diagnosis.[4]

Blood/laboratory tests

- A reduced I2S presence with excluded multiple sulfatase deficiency of the other lysosomal enzymes is indicative of Hunter syndrome.[4]

Genetic testing

- This is the only way to test for carriers of Hunter syndrome mutation.[4]
- Genetic counselling could be beneficial following a diagnosis.[3]

MULTIDISCIPLINARY MANAGEMENT OF HUNTER SYNDROME

"Management of the disease demands that the physician be aware of the special issues surrounding the patient with Hunter syndrome and that a multidisciplinary approach should be taken." - **Dr David Whiteman**

Hunter syndrome is best managed with a multidisciplinary team (MDT) comprised of a number of specialists including, but not limited to:[1]

Gastroenterologist

Gastroenterologists may support with any clinical issues relating to an enlarged liver and spleen, or abdominal hernias.[1]

Geneticist

These physicians can inform other specialists of the genotype of the mutation and educate the family on the need to screen other individuals for Hunter syndrome mutations.[3]

Rheumatologist

The rheumatologist helps to manage manifestations such as claw-like hands, joint contractures and gait problems.[3]

Paediatrician

The paediatrician is often the first point of contact for family members if a new issue arises.[3]

Cardiologist

Cardiovascular complications, such cardiac valve disease, is a common symptom of Hunter syndrome. It would therefore be beneficial to regularly monitor cardiac disease progression.[3]

ENT

This specialist may be the first physician to recognise the syndrome. They may carry out otological and audiological evaluations annually and monitor respiratory involvement.[1]

Neuropsychologist

The neuropsychologist will perform assessments and provide management for Hunter syndrome patients with neuronopathic involvement, such as behavioural problems, cognitive impairment, or more advanced neuronopathic symptoms.[1]

RESOURCES

A range of informative resources are available:

HUNTERSYNDROME.INFO

Huntersyndrome.info is an informative online reference for healthcare professionals interested in all aspects of Hunter syndrome. A range of information about Hunter syndrome is available, including downloadable resources for offline use. Please visit **https://takeda.info/hshcp1**

PODCAST SERIES

Learn at your leisure with the Hunter syndrome podcast series. Episodes include information about MPS diseases, the signs and symptoms of Hunter syndrome, insights on the long journey to diagnosis for many patients, and much more. To download the series, please visit **https://takeda.info/hspodcast**

YOUTUBE SERIES

Learn about all aspects of Hunter syndrome from a range of videos featured on the Hunter syndrome YouTube channel. The channel includes introductory videos, interviews with experts in the field, advanced lectures for more experienced healthcare professionals, and more. To view the channel please visit **https://takeda.info/hsyoutube**

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