FACTS about Atypical HUS

aHUS Awareness Day 2021 - Answers to FAQs

Finding information about any rare disease is challenging, and perhaps more so for an ultra rare disease such as atypical hemolytic uremic syndrome (often shortened to atypical HUS or aHUS) which affects only a handful of people per million.

Created by the aHUS Alliance in 2015 to share information and to raise awareness, aHUS Awareness Day occurs annually on 24 September and provides an opportunity for people and groups around the world to gain insight and understanding for issues key to the atypical HUS community. The theme for the 2021 aHUS Day campaign has been 'United in Advocacy' and among its resources is this, our annual aHUS Fact Sheets.

Since medical knowledge is continually evolving, information that's outdated is cause for concern. The aHUS Alliance Global Action team provides these FAQs (Frequently asked Questions) with current and accurate answers to the most commonly asked questions by patients and aHUS families.

What is atypical HUS?

How many people have atypical HUS?

What causes atypical HUS? Are there different types of aHUS?

What are the symptoms of aHUS?

How is atypical HUS treated?

Is there a cure for atypical HUS? How long is a person treated for aHUS?

There seems to be little advocacy effort or awareness about atypical HUS, what can be done?

What is atypical HUS?

Atypical HUS is short for ‘atypical hemolytic uremic syndrome’ and further abbreviated to aHUS. Often classified as a rare genetic renal (kidney) disease or grouped in treatment with blood disorders, it's not to be confused with the more common HUS, sometimes in the news as an outbreak of food-borne illness or caused by e. Coli infection. An estimated 10% of HUS cases are atypical HUS.

The roots of its name describe the disease: ‘atypical’ (uncommon), ‘hemolytic’ (the destruction of red blood cells), ‘uremic’ (kidney damage due to tiny clots in small blood vessels), and ‘syndrome’ (group of symptoms). This clotting action (thrombotic microangiopathy, TMA) may occur anywhere in the body, so people with atypical HUS can experience damage to major organs other than the kidneys. Atypical HUS may occur as isolated episodes or can be a chronic illness, both with wide variations in severity and duration of illness.

More on this Topic

Research:

C Loirat & V Frémeaux-Bacchi, 2011. *Atypical Hemolytic Uremic Syndrome*

Noris M et al, 20216. *Genetic Atypical Hemolytic-Uremic Syndrome*

aHUS Alliance Articles:

Is it aHUS? Perhaps it’s TTP, STEC-HUS, or Another TMA

Atypical HUS 1.0

How many people have atypical HUS?

Only a handful of people per million have atypical HUS (aHUS, or atypical hemolytic uremic syndrome).

Just as various nations define “rare disease” differently to make specific facts somewhat vague and confusing, data about atypical HUS varies and this, combined with differences in regions and classification of aHUS cases, make atypical HUS statistics difficult to pin down. Since there is not a centralized center coordinating data in the USA, as opposed to EU organizations such as ERKnet, Europe has the largest aHUS reference population.

If you’re looking for how many new cases of atypical HUS occur yearly that is termed disease ‘Incidence’, and in Europe aHUS incidence ranges between 0.23 and 1.9 per million annually. The number of existing cases, or total of new and previous ones at any given point in time, is called disease ‘Prevalence’, and in Europe prevalence of aHUS is 4.96 per million total population.

More on this Topic:

Research (and detailed statistics): Yan et al (2020) *Epidemiology of Atypical Hemolytic Uremic Syndrome: A Systematic Literature Review*

aHUS Alliance Articles:

Again, just how Many aHUS Patients are There?

Know aHUS: Know Us (EN, FR, ES)

What causes atypical HUS? Are there different types of aHUS?

Atypical HUS is sometimes referred to as 'familial aHUS' due to genetic flaws which can run in families. This abnormality or predisposition for atypical HUS, within a person's DNA at birth, is increasingly called 'primary aHUS' but it may remain dormant or can become active or 'triggered' at any age. Genetic screening may indicate a specific issue, but aHUS can be 'ideopathic' and arise spontaneously or from an unknown cause.

Known genetic causes of aHUS are complement regulatory genes (C3, CFB, CFH, and related genes, CFI, CD46), which is why it's sometimes referred to as 'complement mediated aHUS'. We're still learning why the part of the body's immune response, the complement system, becomes overactive and unregulated which in turn can negatively impact body functions and cause organ damage. There are other forms and classifications of atypical HUS, which adds to the confusion and makes information difficult to sort through. Other genetic causes of aHUS are mutations regarding THBD and DGKE genes.

Sometimes outside factors and other health issues can cause aHUS activity to occur. Classified by some as 'Secondary aHUS', triggers for atypical HUS can include infection or inflammation, pregnancy (p-aHUS), malignancy (cancers), autoimmune diseases, and some medications. This overlap of causes and scenarios can make diagnosis of aHUS quite difficult, as there is no specific test to distinguish atypical HUS from other conditions with similar symptoms (such as HUS,TTP, or other syndromes of thrombotic microangiopathies like aHUS).

There are current projects underway for clinicians and research teams to be more specific in defining different types of TMA, which will provide better understanding of how best to treat aHUS caused by different circumstances.

More on this Topic:

Research:

Bernabeu et al (2020) Atypical Hemolytic Uremic Syndrome: New Challenges in the Complement Blockage Era

Ardissino et al (2021) Risk of Atypical HUS Among Family Members of Patients Carrying Complement Regulatory Gene Abnormality

aHUS Alliance Articles:

When Good Complement goes aHUS Bad

aHUS - Is its End really Nigh?

What are the symptoms of aHUS?

Atypical HUS is a condition that affects the blood and blood vessels. It results in the destruction of red blood cells (cells involved in carrying oxygen around the body) as the lining of small blood vessels shear them apart. Decline in red blood cell (RBC) counts mean many aHUS patients experience marked fatigue (tiredness) due to anemia. Damage to the body's small blood vessels cause platelets to respond and form repairs, but formation of these tiny clots throughout the body deplete the blood's platelet counts (thrombocytopenia) and cause aHUS patients to bruise more easily. These tiny clots clog blood vessels, especially in the kidneys, and damage organ function.

No two cases of atypical HUS are alike, even for people with the same genetic mutation nor even within families whose screening results indicate the same genetic predisposition for atypical HUS. Symptoms of aHUS vary, but include hemolytic anemia (destruction of red blood cells), low platelets (consumed by clot formation), and organ damage due to tiny blood clot formation in capillaries and small arteries (thrombotic microangiopathy, TMA). Atypical HUS symptoms may appear in a vague and gradual manner (nausea, tiredness, lack of appetite), or with sudden and life-threatening impact (stroke, seizure, cardiac event). It may occur in the form of episodes (sporadic) or continue ongoing activity and become a chronic illness. Patients with aHUS may experience wide-ranging issues with a variety of body systems and organs: kidneys, heart, lungs, peripheral & central nervous system, skin, eyes, and GI tract.
According to one source (Scully et al, 2016), atypical HUS patients newly enrolled in the global aHUS registry experienced these types of issues within 6 months of disease onset: renal (75%), gastrointestinal (38%), cardiovascular (32%), central nervous system (25%), and pulmonary (19%).
Given that complexity, medical care for aHUS patients should incorporate a cross-discipline team approach for treatment.

More on this Topic:
Research:
Hofer et al (2014) *Extra-renal manifestations of complement-mediated thrombotic microangiopathies*
Scully et al (2016) *Systemic Involvement at Entry into the Global Atypical Hemolytic Uremic Syndrome (aHUS) Registry*
aHUS Alliance Articles:
aHUS Better - It Depends & It takes Time
aHUS Patient Care – the Need for Multidisciplinary Collaboration

How is atypical HUS treated?
As of 2020 there are two medications that treat atypical HUS, eculizumab (brand name, Soliris) and ravulizumab (brand name, Ultomiris) which are both products of Alexion, AstraZeneca Rare Disease. Less than a third of nations have rare disease policies or orphan drug regulations which allow high-cost biopharmaceuticals, so most physicians cannot treat the disease with these drugs. For a majority of the world's adults and children who have aHUS, treatment falls back to plasmatherapies, which include plasma exchange and plasma infusion.

Therapeutic plasma exchange (PE, PLEX, or TPE) otherwise known as 'plasmapheresis' (sometimes shortened to pheresis or apheresis) removes the patient's plasma and replaces it with plasma from a blood donor (fresh frozen plasma, FFP) while filtering out and removing abnormal factors. Plasma infusion does not require the specialized machine or central line like plasmapheresis, but involves an IV infusion of donor plasma which in theory may bolster abnormal complement factors. Plasmatherapies are designed to support the patient, but do not treat or halt the disease.
Development of more therapeutic drugs to treat atypical HUS, with a current expansion of new drugs now in pharma research pipelines and in clinical trials, will prevent kidney failure as well as loss of aHUS lives. Atypical HUS families will play an important role in working with physicians and others to advocate for drug access within their own nations.

More on this Topic:

Research:

Lee et al (2020) *Consensus regarding diagnosis and management of atypical hemolytic uremic syndrome*

Goodship et al (2017) *Atypical hemolytic uremic syndrome and C3 glomerulopathy: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference*

aHUS Alliance Articles:

The Reluctant Advocate

aHUS Drug Access Panel - Proposed Model

Is there a cure for atypical HUS? How long is a person treated for aHUS?

At its most basic roots, atypical HUS usually occurs in people with one or more genetic errors. Since our genes (DNA) are found in almost every cell throughout the body, science has no current way to change or cure aHUS. A person with a genetic predisposition for atypical HUS may never experience its damaging episodes, while in others it may trigger during infant years and still others find it may lie dormant until late adulthood.

Treatment length for people with aHUS is highly variable, dependent on factors including but not limited to: the person's overall health, what other medical conditions or circumstances are in play (pregnancy, COVID-19 infection, auto-immune diseases), and organ functions impacted by aHUS (kidney failure, heart issues, seizure activity, memory or cognitive difficulties, GI tract pain, or complications involving the lungs, skin or eyes).

Out of an estimated 7,000 different rare diseases, people with atypical HUS are among the mere 5% of rare disease groups with an approved drug, device, or treatment. Plasmatherapies (infusion or exchange) can alleviate the symptoms for some aHUS patients but do not halt the disease. While there are 2 drugs approved to treat aHUS in several countries, they are available to only an estimated 1/4 to 1/3 of the world's aHUS patients. Drug cost drives drug access for healthcare in most nations, and affordability can greatly impact treatment for those with atypical HUS.

The trend toward 'personalized medicine' and individual care exemplifies treatment goals for all aHUS patients around the world, a multidisciplinary team approach to provide the right drug(s) for the right length of time. For those patients discontinuing treatment with complement inhibitors (eculizumab or ravulizumab) there are risk factors to consider, given that atypical HUS can relapse and occur unexpectedly, so there are essential and individualized points to discuss between patients and their medical teams. International study groups and research teams are currently working to determine such guidelines, to include clinical trials and collaborative efforts in France, the Netherlands, the UK, and other nations.

More on this Topic

Research: Available by Topic

aHUS Research & Publications - Hundreds available in our Info Centre, see lists for specific Topics such as: Treatment, Relapse Risk/Discontinuing Treatment, Extra Renal (Effects on the Body) & several more Categories

aHUS Alliance articles:

Withdrawal - a Need for Consensus

Thrombotic Microangiopathy & Precision Medicine

There seems to be little advocacy effort or awareness about atypical HUS, what can be done?

Rare disease information seems in short supply for a very logical reason - few people are affected so time and resources are usually dedicated to medical issues which affect large patient numbers. People who are most directly affected by an issue are among the first or most deeply dedicated to become involved in speaking or writing about that topic, and in searching for solutions or pathways forward. That's certainly true for aHUS patients, the medical professionals who treat them, and for the friends and families of people living with atypical HUS.

In 2015, 24 September marked the inaugural date for the 1st international aHUS Awareness Day marking 60 years since Dr Conrad von Gasser's team coined the term 'HUS' to describe an illness which caused blood clotting, anemia and kidney failure. Since then progress has been made with international collaborations to study and publish aHUS research, to create patient registries and genetic databases, and to establish of aHUS/TMA study centers in various parts of the world. Medical societies, hospitals, and universities are beginning to offer more 'MedEd' events on thrombotic microangiopathies such as atypical HUS but few include aHUS patient views and experiences.

With just a handful of aHUS patients per million people, atypical HUS advocacy requires a strong grassroots movement of patient engagement. Unlike other medical conditions with large organizations which retain paid staff to provide information and support programs, the aHUS arena relies on volunteers around the world to provide an independent and authentic voice for aHUS issues. Expanding aHUS drug access and changing rare disease policies often begins with patient families working together with clinician/researchers.

It will take the collaboration and commitment of people and groups to fill in current aHUS knowledge gaps. At the core of patient treatment, caregiver concerns, medical team coordination, and disease research lies exchange and communication of information and issues. People living with aHUS, along with their friends and family, need to take an active role and engage with aHUS advocacy efforts by dedicating time to share information and awareness for this very rare disease. Progress in developing aHUS treatments that are effective, affordable, and available to patients around the world is at the heart of aHUS awareness and advocacy.

More on this Topic

Research:

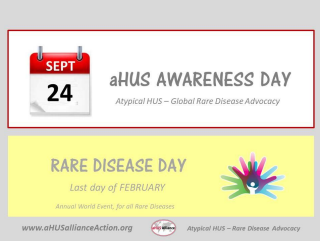
Raina et al. (2019) *Optimal management of atypical hemolytic uremic disease: challenges and solutions*

Woodward et al (2016) *An innovative and collaborative partnership between patients with rare disease and industry-supported registries: the Global aHUS Registry*

aHUS Alliance articles:

Atypical HUS: What are You Waiting For?

Global aHUS Advocacy



aHUS Awareness Day - an annual 24 Sept campaign

Founded by the aHUS Alliance in 2015 and recognized each 24 September, aHUS Awareness Day was designed to raise visibility of rare disease healthcare for aHUS patients, to highlight atypical HUS research, shed light on treatment issues facing physicians and patients, and provide insight into the needs of people living with atypical HUS.

Our global aHUS Awareness Day campaign each year includes disease-specific resources and updated, objective information for use in all nations and by all stakeholders.

Rare Disease Day - recognized the last day of February

Rare Disease Day was founded in 2008 by EURORDIS to raise awareness for the people affected by rare medical conditions and for the issues and challenges faced by patients and their families. Atypical HUS is one of an estimated 7000+ rare diseases, individually uncommon but collectively affecting perhaps an estimated 1 in 12 people. Rare diseases are defined differently around the world, so Rare Disease Day facts vary. While exact numbers of people diagnosed with aHUS are unknown, it affects only a handful of people per million and as such is an ultra-rare disease.

As umbrella organization of aHUS advocates and patient groups in over 30 nations, the aHUS Alliance annually participates in world Rare Disease Day with articles, graphics, and projects with a specific focus on atypical HUS.

Visit our website www.aHUSallianceAction.org for more info & resources

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