A PATIENT'S JOURNEY

Learning about atypical hemolytic uremic syndrome (aHUS)

ALEXION®

Begin your path to empowerment

Being diagnosed with aHUS can be overwhelming. You may have many questions: What is aHUS? How did I get it? Who can I turn to for help? This brochure will help you learn more about your diagnosis of aHUS and will guide and support you on this lifelong journey.

Even though aHUS is a rare disease, you are not alone.

Let's get started...

"When I was first diagnosed with aHUS, I wasn't sure what to do. Finding the right resources, team, and support network helped me feel like I wasn't alone." – Patient diagnosed with aHUS

A PATIENT'S JOURNEY

Learning about aHUS

The journey begins: What is aHUS?

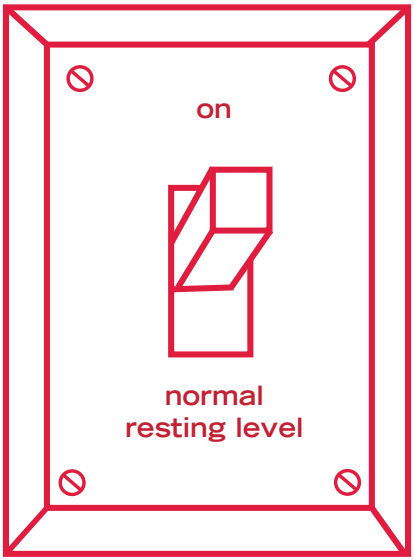
aHUS is a disorder caused by a genetic change (such as a **mutation**) in the **complement system**, which is part of the immune system.[1,2] The complement system is always "on" at a low level and ready to increase activity to protect you from infection.[3,4] Everyday occurrences, including infection, allergy, and even pregnancy, can increase complement activation.[2,5–10]

Normally, your body is able to recognize when complement levels should return to normal. In people with aHUS, the body has a problem regulating complement which causes it to be uncontrolled due to the changes in the complement regulatory genes.[1,3,6]

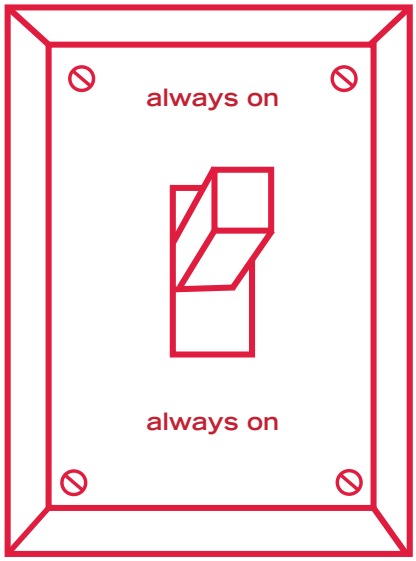
Will I always have aHUS?

aHUS is a genetic disease that is caused by a change, or mutation, in your DNA.[1–3] This means that you will always have aHUS.[1] These mutations make it difficult for your body to regulate, or "turn off," the complement system.[2,11,12] **Research is ongoing and more information can be found at www.aHUSSource.com and www.clinicaltrials.gov.[8,13] Be sure to speak with your doctor about management options for patients with aHUS that are available now.**

Complement activity can be increased by everyday occurrences such as a bacterial or viral infection, pregnancy, allergy, and other trauma.[2,5-9]



versus



In people without aHUS:

The complement system is turned on by everyday occurrences.[3] After the need is gone, the body regulates the complement system by turning it to normal levels.[1,3,6]

In people with aHUS:

The body cannot regulate the complement system.[1,14] It remains turned on, or "activated."[1,3] This uncontrolled complement activation can cause damage to many parts of the body.[15-19]

What you may encounter on your journey: Signs and symptoms of aHUS

When you have aHUS, increased complement activity can lead to damage of cells along the blood vessel walls and **platelets** becoming overactive.[5,18,20] This can result in blood clots that form in the small vessels that go to the kidneys, heart, brain, digestive tract, and other organs causing harm or impairment.[6,18,20]

You may have already experienced some of the symptoms listed below. If you think you are experiencing any of these symptoms, contact your doctor right away. Understanding aHUS and recognizing its signs and symptoms are important steps in managing the effects of the disease.

KIDNEYS

>50% of all patients with aHUS have kidney complications

- Dialysis (**end-stage renal disease**)[25]

BRAIN

48% of patients with aHUS have **neurologic** symptoms[16]

- Confusion[21]
- **Stroke**[21]
- **Seizure**[16]

"I was under the impression that aHUS is a blood disease that involves only your kidneys... I didn't realize the brain and heart can also be involved." – Patient diagnosed with aHUS

HEART

43% of patients with aHUS have **cardiovascular** symptoms[16]

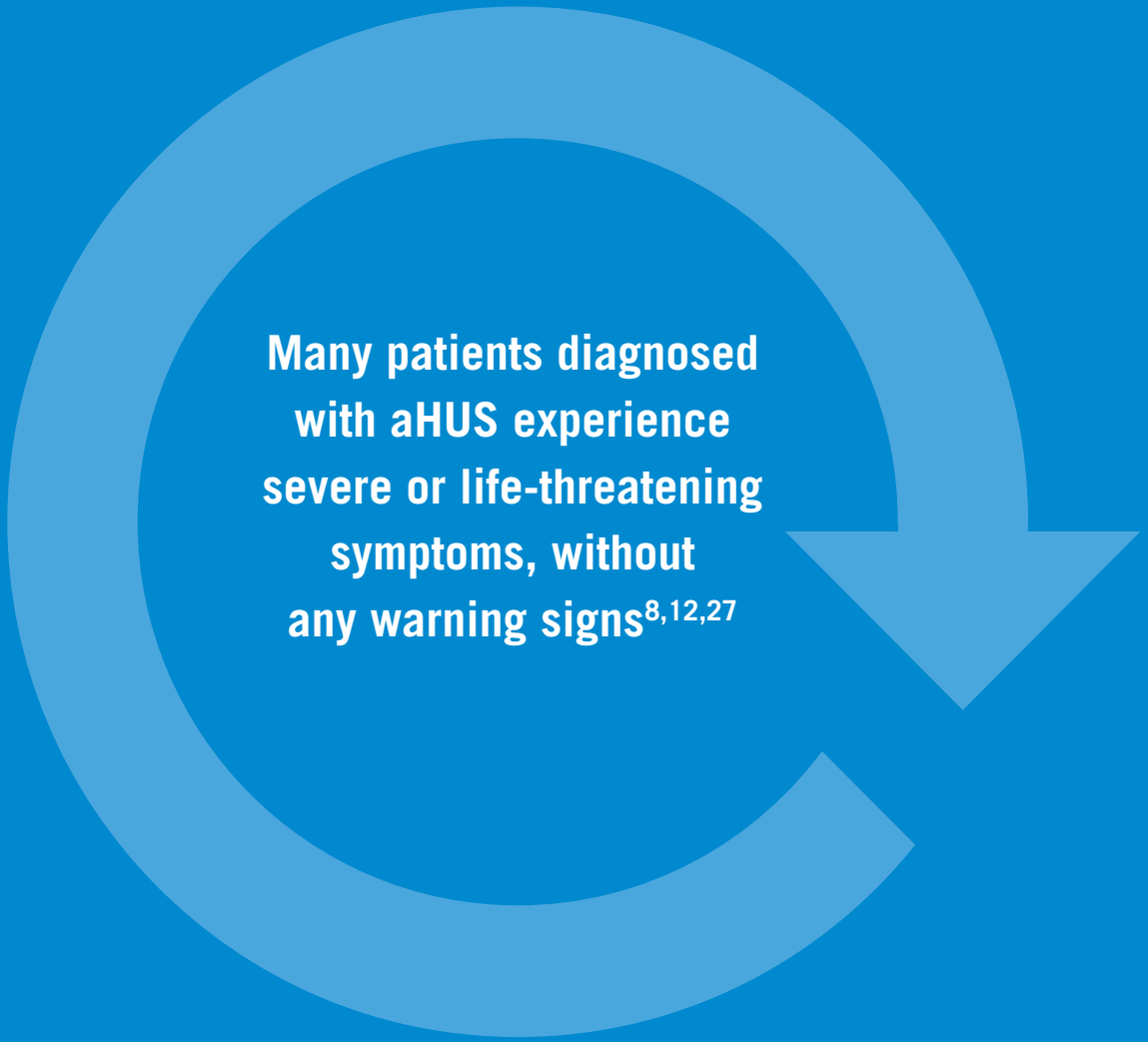
- Heart attack[19,22]
- High blood pressure/**hypertension**[23]
- Blood clots[18]

DIGESTIVE TRACT

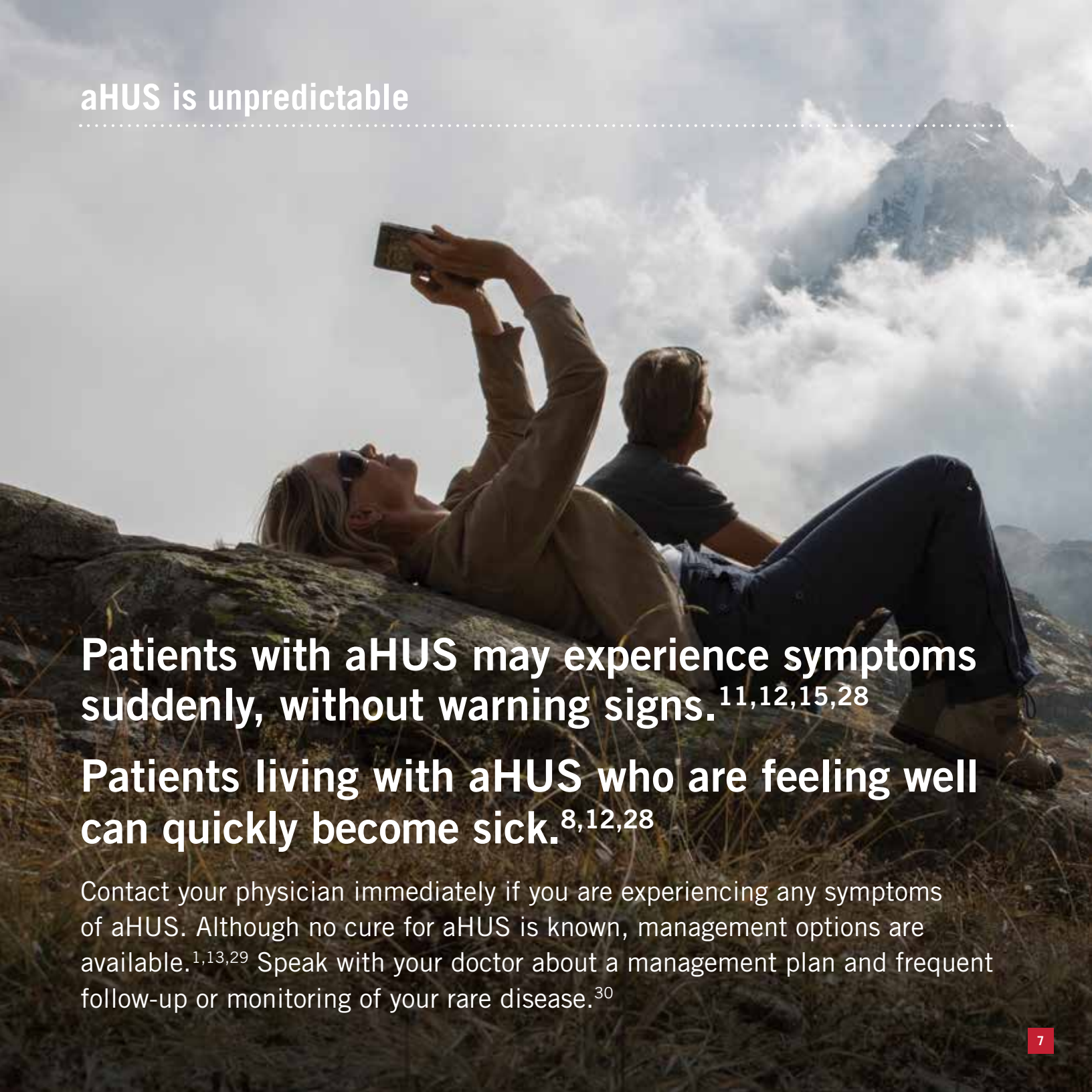
37% of patients with aHUS experience gastrointestinal symptoms[18]

- Abdominal pain[20]
- Diarrhea[10,24]
- **Colitis**[25]
- Nausea/vomiting[26]

aHUS is a chronic disease



Every person with aHUS is different. Some may go for long periods without symptoms, but others may feel sick frequently.[1,27]



Patients with aHUS may experience symptoms suddenly, without warning signs.[11,12,15,28]

Patients living with aHUS who are feeling well can quickly become sick.[8,12,28]

Contact your physician immediately if you are experiencing any symptoms of aHUS. Although no cure for aHUS is known, management options are available.[1,13,29] Speak with your doctor about a management plan and frequent follow-up or monitoring of your rare disease.[30]

"Support is available at the time of diagnosis and will continue as you manage aHUS."

– Patient diagnosed with aHUS

Getting oriented: Talking with your doctor

Here are a few questions you may want to consider asking your physician:

How will we manage my aHUS?

What are my treatment options?

What kind of care will I need at home, if any?

How often will I need to see a doctor?

What tests will be done when I see the doctor? What will the results tell me?

What are important signs and symptoms that I should monitor when I go home?

If I'm not feeling well, who should I call?

Currently, no cure for aHUS is known, but you and your doctor can take steps to reduce the risk of serious consequences.[1,13,29]

Staying on track: Managing aHUS and getting the support you need

Being diagnosed with aHUS may bring changes to your daily life, including some challenges. Along with physical changes, you may feel many emotions after you are diagnosed with aHUS. It's important to know that there are people you can turn to for support.

"It does get better. It's scary at first, but it does get better."

- Patient diagnosed with aHUS

Your first step in managing aHUS will likely be to start to build a partnership with your health care team. This team may include your doctor and nurses and other members of the office staff. Team members can answer questions that you may have about aHUS and management options. Along with your health care team, a variety of resources are available to provide support for you and for your family.

You may find it helpful to talk to other patients and families dealing with aHUS. Although the exact path is different for everyone, other aHUS patients are on a journey that may be similar to yours. Several groups and foundations can serve as valuable resources for patients, as well as caregivers.

OneSource™ is a program that will connect you with Alexion Nurse Case Managers who are experienced in working with patients with aHUS. Keep reading to find out more about this valuable program.

ONESOURCE™
TREATMENT SUPPORT

Living with aHUS can be a challenge:
Although aHUS is rare, support is not hard to find.

OneSource is available to provide essential support, regardless of the management plan you choose.

- OneSource is a complimentary program offered by Alexion
- OneSource is staffed by Case Managers: registered nurses with clinical knowledge and funding expertise
- OneSource can help patients facilitate the transition from hospital to home
- OneSource Case Managers are assigned geographically, so they are familiar with physicians, hospitals, community resources, and funding options unique to your area

OneSource Case Managers provide ongoing support in the following areas:

- **Education**: Collaborating with your healthcare team, to answer questions, and provide educational materials related to aHUS
- **Coverage issues and funding options**: Assisting patients and practices with insurance coverage questions and researching funding options
- **Management support:** Assisting with solutions for balancing all aspects of disease management when faced with major life challenges, such as college, relocation, marriage or divorce, retirement, or changes in insurance coverage

"This disease is very rare. But it's not rare to me."

– OneSource Nurse Case Manager

"If I needed information or had questions, I would contact OneSource... it is a support system, a way to make sure you don't fall through the cracks."

– Patient diagnosed with aHUS

Call OneSource at 1.888.765.4747 to speak one-on-one with a OneSource Case Manager. Case Managers can assist you with educational resources and information about funding options and assistance.

To learn more about OneSource, visit www.ahussource.com/Patient/OneSource

Support groups: Find other people who are living with aHUS

A diagnosis of aHUS can feel overwhelming. Below are some resources that can provide additional guidance.

aHUSSource
atypical Hemolytic Uremic Syndrome (aHUS)

aHUS Source

Provides patients and caregivers information on aHUS, along with a guide to help you and your doctor work together to manage aHUS. You can also access OneSource™, where you can speak with a registered nurse to ask questions about aHUS.

Website: www.ahussource.com

Genetic and Rare Diseases Information Center (GARD)

Helps people find information about genetic and rare diseases. Information Specialists are available to talk with you about aHUS in both English and Spanish.

Website: www.rarediseases.info.nih.gov/GARD

The Atypical HUS Foundation

A volunteer organization open to patients, family, friends, caregivers, researchers, and medical personnel. The Foundation encourages patients and researchers to share information and their personal experiences to foster a better understanding of aHUS. The overall goal is to gather people together to improve the lives of patients and families dealing with aHUS.

Website: www.atypicalhus.ning.com

The Global Genes Project

An organization that works to meet the needs of people living with rare diseases. This organization aims to build awareness of rare diseases and to provide resources and connections to patients and their families. The Global Genes Project hosts meetings for patients with aHUS and their families across the country.

Website: www.globalgenes.org

Support for people living with aHUS

OneSource is a personalized program that provides education, case management, and support for patients and their caregivers. OneSource is staffed by Alexion Nurse Case Managers, all of whom are registered nurses with extensive clinical experience.

Website: www.ahussource.com/Patient/OneSource

National Organization for Rare Disorders (NORD)

NORD is dedicated to helping people with rare, or "orphan," diseases. This organization helps patients access assistance programs for medication. They host meetings for patients with aHUS and their families to help them connect to others and provides information on rare diseases by sharing patients' personal stories.

Website: www.rarediseases.org

Glossary

Basic metabolic panel (BMP) is a set of blood chemical tests (ie, Chem-7 or Chem-10) that provides key information regarding fluid and electrolyte status, kidney function, blood sugar levels, and response to various medications. It is frequently employed as a screening tool during a physical exam.

Cardiovascular means involving the heart and/or blood vessels.

Colitis is swelling or inflammation in the large intestine, or colon.

Complement system is a natural part of the immune system that helps protect the body from foreign substances like bacteria or other infections. The complement system is made up of a group of proteins found in the blood.

Complete blood count (CBC) is a blood panel test that measures red blood cells, white blood cells, hemoglobin, and platelet count to provide a broad view of the cells in a patient's blood. This test can help your doctor diagnose abnormalities and evaluate cell production and breakdown.

Creatinine is a chemical waste molecule that is generated through muscle metabolism and is transported through the bloodstream to the kidneys. Creatinine has been found to be a fairly reliable indicator of kidney function; an elevated creatinine level in the blood can signify impaired kidney function or kidney disease.

End-stage renal disease (ESRD) occurs when the kidneys can no longer function to remove waste and excess water from the body. Patients with ESRD must undergo hemodialysis to filter their blood.

Endothelial cells form the inner lining of a blood vessel and provide an anticoagulant barrier between the vessel wall and the blood. These cells are involved in the immune response, blood clotting, inflammation, blood pressure, and organ repair.

Genetic disease is a disease caused by a genetic mutation.

Hematologist is a doctor who specializes in treating patients with diseases involving the blood.

Hemodialysis is a procedure used to filter blood when the kidneys are not functioning properly. Blood flows through a filter that removes waste and water, and then is returned to the body.

Hemoglobin is the protein molecule in red blood cells that carries oxygen from the lungs to body tissues and returns carbon dioxide from the tissues to the lungs.

Hemolytic anemia is a condition in which red blood cells are destroyed and removed from the bloodstream before their normal lifespan is over. When blood cells die, the body's bone marrow makes more blood cells to replace them. However, in hemolytic anemia, the bone marrow cannot make red blood cells fast enough to meet the body's needs.

Hypertension is another term for high blood pressure.

Lactate dehydrogenase (LDH) is an enzyme that is found in almost all of the body's cells and is released from cells into the blood when cells are damaged or destroyed. Thus, the blood level of LDH is a general indicator of tissue and cellular damage.

Mutation is a permanent change in the DNA sequence that makes up a gene. Genes code for proteins, so changes that occur in the DNA sequence can lead to proteins that do not function properly.

Nephrologist is a doctor who specializes in the kidneys and in kidney diseases.

Neurologic means involving the nervous system, including the brain, spinal cord, and nerves.

Platelets (or thrombocytes) are blood cells whose function is to help the blood clot to stop bleeding.

Proteinuria is a condition in which urine contains abnormal amounts of protein. As blood passes through healthy kidneys, they filter out waste products and leave in proteins and other things the body needs. However, proteins from the blood can leak into the urine when the filters of the kidney are damaged. Proteinuria is a sign of kidney disease.

Red blood cells (or erythrocytes) are the most common type of blood cell. They contain hemoglobin and are the body's principal means of delivering oxygen to body tissues via the circulatory system.

Seizure is caused by changes in the activity of nerve cells within the brain. Seizures can vary in intensity from barely recognizable events to loss of consciousness and convulsions.

Stroke is a medical emergency caused by lack of blood flow to the brain, causing death of brain cells.

Thrombosis is the formation of a blood clot inside a blood vessel. This leads to a blockage in the flow of blood through the blood vessels.

Thrombotic microangiopathy (TMA) is a disorder that results in clots and inflammation in various small blood vessels throughout the body, due to an endothelial injury.

Urinalysis is the physical, chemical, and microscopic examination of urine. It involves several tests that detect and measure various compounds that pass through the urine.

White blood cells (or leukocytes) are the cells of the immune system that are involved in defending the body against disease. White blood cells are produced in the bone marrow and are found throughout the blood and lymphatic system. The number of white blood cells in the blood is often an indicator of disease.

References

1. Noris M, Remuzzi G. Atypical hemolytic-uremic syndrome. *N Engl J Med.* 2009;361(17):1676-1687. **2.** Noris M, Caprioli J, Bresin E, et al. Relative role of genetic complement abnormalities in sporadic and familial aHUS and their impact on clinical phenotype. *Clin J Am Soc Nephrol.* 2010;5(10):1844-1859. **3.** Holers VM. The spectrum of complement alternative pathway-mediated diseases. *Immunol Rev.* 2008;223(1):300-316. **4.** Zipfel PF, Heinen S, Skerka C. Thrombotic microangiopathies: new insights and new challenges. *Curr Opin Nephrol Hypertens.* 2010;19(4):372-378. **5.** Noris M, Mescia F, Remuzzi G. STEC-HUS, atypical HUS and TTP are all diseases of complement activation. *Nat Rev Nephrol* 2012;8(11):622-633. **6.** Liszewski MK, Atkinson JP. Too Much of a Good Thing at the Site of Tissue Injury: The Instructive Example of the Complement System Predisposing to Thrombotic Microangiopathy. *ASH Educ Program Book* 2011;2011(1):9-14. **7.** Fang CJ, Richards A, Liszewski MK, Kavanagh D, Atkinson JP. Advances in understanding of pathogenesis of aHUS and HELLP. *Br J Haematol* 2008;143(3):336-348. **8.** Campistol JM, Arias M, Ariceta G, et al. An update for atypical haemolytic uraemic syndrome: diagnosis and treatment. A consensus document. *Nefrol Publ Of Soc Esp Nefrol* 2013;33(1):27-45. **9.** Fakhouri F, Roumenina L, Provot F, et al. Pregnancy-Associated Hemolytic Uremic Syndrome Revisited in the Era of Complement Gene Mutations. *J Am Soc Nephrol JASN* 2010;21(5):859-867. **10.** Geerdink LM, Westra D, Wijk JAE van, et al. Atypical hemolytic uremic syndrome in children: complement mutations and clinical characteristics. *Pediatr Nephrol* 2012;27(8):1283-1291. **11.** Loirat C, Fremeaux-Bacchi V. Atypical hemolytic uremic syndrome. *Orphanet J Rare Dis* 2011;6:60. **12.** Fremeaux-Bacchi V, Fakhouri F, Garnier A, et al. Genetics and Outcome of Atypical Hemolytic Uremic Syndrome: A Nationwide French Series Comparing Children and Adults. *Clin J Am Soc Nephrol CJASN* 2013;8(4):554-562. **13.** Kavanagh D, Goodship TH, Richards A. Atypical Hemolytic Uremic Syndrome. *Semin Nephrol* 2013;33(6):508-530. **14.** Zhao J, Wu H, Khosravi M, et al. Association of Genetic Variants in Complement Factor H and Factor H-Related Genes with Systemic Lupus Erythematosus Susceptibility. *PLoS Genet* 2011;7(5):e1002079. **15.** Caprioli J, Noris M, Brioschi S, et al. Genetics of HUS: the impact of MCP, CFH, and IF mutations on clinical presentation, response to treatment, and outcome. *Blood* 2006;108(4):1267-1279. **16.** Neuhaus TJ, Calonder S, Leumann EP. Heterogeneity of atypical haemolytic uraemic syndromes. *Arch Dis Child* 1997;76(6):518-521. **17.** Larakeb A, Leroy S, Frémeaux-Bacchi V, et al. Ocular involvement in hemolytic uremic syndrome due to factor H deficiency--are there therapeutic consequences? *Pediatr Nephrol Berl Ger* 2007;22(11):1967-1970. **18.** Langman C. Systemic Multit-Organ Complications in Atypical Hemolytic Uremic Syndrome (aHUS): Retrospective Study in a Medical Practice Setting. In: *European Hematology Association.*Vol 97. s1. Amsterdam, The Netherlands: Haematologica; 2012:195-196. **19.** Noris M, Remuzzi G. Cardiovascular complications in atypical haemolytic uraemic syndrome. *Nat Rev Nephrol* 2014;10(3):174-180. **20.** Ruggenenti P, Noris M, Remuzzi G. Thrombotic microangiopathy, hemolytic uremic syndrome, and thrombotic thrombocytopenic purpura. *Kidney Int* 2001;60(3):831-846. **21.** Salem G, Flynn JM, Cataland SR. Profound neurological injury in a patient with atypical hemolytic uremic syndrome. *Ann Hematol* 2013;92(4):557-558. **22.** Sallée M, Daniel L, Piercecchi M-D, et al. Myocardial infarction is a complication of factor H-associated atypical HUS. *Nephrol Dial Transplant* 2010;25(6):2028-2032. **23.** Kavanagh D, Goodship THJ, Richards A. Atypical haemolytic uraemic syndrome. *Br Med Bull* 2006;77-78(1):5-22. **24.** Zuber J, Le Quintrec M, Sberro-Soussan R, Loirat C, Frémeaux-Bacchi V, Legendre C. New insights into postrenal transplant hemolytic uremic syndrome. *Nat Rev Nephrol* 2011;7(1):23-35. **25.** Hirt-Minkowski P, Dickenmann M, Schifferli JA. Atypical Hemolytic Uremic Syndrome: Update on the Complement System and What Is New. *Nephron Clin Pract* 2010;114(4):c219-c235. **26.** Dragon-Durey M-A, Sethi SK, Bagga A, et al. Clinical Features of Anti-Factor H Autoantibody-Associated Hemolytic Uremic Syndrome. *J Am Soc Nephrol JASN* 2010;21(12):2180-2187. **27.** Loirat C, Garnier A, Sellier-Leclerc A-L, Kwon T. Plasmatherapy in atypical hemolytic uremic syndrome. *Semin Thromb Hemost* 2010;36(6):673-681. **28.** Sellier-Leclerc A-L, Fremeaux-Bacchi V, Dragon-Durey M-A, et al. Differential Impact of Complement Mutations on Clinical Characteristics in Atypical Hemolytic Uremic Syndrome. J Am *Soc Nephrol* 2007;18(8):2392-2400. **29.** Scheiring J, Rosales A, Zimmerhackl LB. Clinical practice. *Eur J Pediatr* 2009;169(1):7-13. **30.** Bitzan M, Schaefer F, Reymond D. Treatment of typical (enteropathic) hemolytic uremic syndrome. *Semin Thromb Hemost* 2010;36(6):594-610.