The Foundation for Children with Atypical HUS

A Parent's Perspective - aHUS BOOTCAMP

You or your child have been diagnosed with Atypical HUS - Now What?

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So, you or your child's symptoms have lead you to the doctor or straight to the hospital. Symptoms may have included extreme fatigue, puffiness, vomiting, paleness, fever, and perhaps some diarrhea. It is possible that you noticed swelling as well as dark or strong smelling urine. Your child's appetitie may have completely vanished and you are struggling to get him or her to eat. Since the medical diagnosis of atypical HUS (hemolytic uremic syndrome) you're now hearing terms like schistocytes, blood smears, platelets, red and white blood cell counts, and protein in the urine! What does it all really mean?

Types of Hemolytic Uremic Syndrome (HUS) There are two types of HUS: typical HUS (caused by E coli or other othen food/water borne pathogens) and atypical HUS (usually a genetic mutation but sometimes triggered by other illnesses or even by unknown causes)

***HUS (Typical HUS)** Typical HUS can be triggered by E coli bacteria or other, often food borne pathogens (such as with the 2007 contaminated spinach outbreak). This can cause an immune system response that causes hemolysis (shattering of red blood cells) and kidney failure. In typical HUS, most cases will not occur again after the initial onset (typically lasting 4-6 weeks). Cases can see long-term kidney damage and issues with high bloood pressure.

***atypical HUS** Atypical HUS can be triggered for a variety of reasons such as genetic mutation, pneumonia, or gastro-intestinal illness - as well as unknown reasons (ideopathic). The biggest difference between types is that atypical HUS is unpredictable and can/will relapse or recurr with some frequency. It is estimated that there are from 300 to 600 aHUS patients in the United States, most of them young children, but each case is quite different. Some cases will relapse intermittently - often triggered by exposure to a virus- while others have chronic symptoms and never truly reach remission. Some relapses are relatively mild and easily controlled while other aHUS events come on devastatingly quick.

What happens to the body during the attack?

With aHUS the red blood cells break apart and these cell fragments travel to the kidneys, making tiny microscopic clots causing severe anemia and kidney failure. When the kidneys fail to work, the body fails to rid itself of toxins, the urine output declines, and the amount of protein in the urine will increase. This process can permanently damage the kidneys. Poorly functioning kidneys also lead to high blood pressure and swelling which can stress the heart and lungs. In rare cases blood clots

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may develop somewhere else in the body, with some aHUS patients also experiencing neural events such as seizure activity. Platelets are consumed during aHUS activity and LDH levels will rise, so lab tests must be ordered to give the physican an overview of the disease process. Treatment will be determined by lab test results, so expect blood draws to be ordered by your doctor and their results to discussed with you (CBC, BMP, and LDH are lab tests commonly ordered).

About the Doctors

Atypical HUS is a very rare disease, estimated at 300 to 600 cases in America and about 1000 patients worldwide. Having knowledgeable specialists is critical for successful treatment, though due to the rarity of this disease few doctors have experience with treating another aHUS case. Typically these are the types of doctors that will be primarily involved in an aHUS case (although others may be consulted): **Nephrologists** are experts of kidney dieases. This doctor will monitor kidney function, electrolytes, blood pressure, disease activity, and dialysis (when necessary). Kidneys are very sensitive organs and care can be complex/difficult due to the wide range of issues. This doctor should be a primary link for aHUS cases and should be heavily involved in a patient's treatment and care plan. **Hematologists** are experts in blood diseases. This doctor will closely monitor aHUS activity and its' effects on the body's blood. Sometimes a consulting physican may be an **oncologist**, a doctor who specializes in cancer and who may asked for their opinion on other blood diseases. Many hospitals place aHUS in the care category of nephrologists, still others choose to send aHUS cases to hemotolgists. Physicans entrusted with aHUS cases must have expertise in both kidney and blood aspects.

Treatment Types

Be aware that aHUS cases DO NOT have a standard 'treatment protocol' as is common in most other diseases. Due to the complexity and variability of aHUS symptoms, expect that your physician will try one or more of the options below and await lab results to see the degree of treatment's effectiveness. Some patients respond well to one treatment type chosen, while others' lab work will indicate that another treatment yields better lab values. Blood samples drawn from the aHUS patient will yield lab test results, the critical keys that determine treatment type and frequency. Some aHUS patients who do not respond to plasma products may respond to treatments that target the immune system. Sometimes **IVIG (intravenous immune globulin**) is used in conjunction with, or instead of, plasma products. IVIG is a man-made blood product that can help to regulate the immune system. **Steroids**, such as Predisone, are also sometimes effective but can lead to increased blood pressure in aHUS patients and should be used only under very close medical care. Due to the ongoing nature of the disease process and subsequent damage to the kidneys, nearly all aHUS patients will need some kind or combination of

blood pressure medication. Managing **high blood pressure (hypertension)** is critical to keep the heart and kidneys from being stressed.

***Blood Transfusions**: Some type of blood product transfusion is almost always the first line of treatment. Typically, aHUS patients are admitted to the hospital with lab tests indicating low red blood cells and low platetlet numbers. Depending on the doctor's decision, a patient may receive packed red blood cells, whole blood, and/or platelets in order to stabilize their current situation. These products help to return the blood to a more normal level for a brief time but do not treat the disease. When blood products are given, doctors have to closely manage fluid levels in the body. If the kidneys are not working properly, the extra fluid can cause stress on the heart and lungs.

***Plasma Therapies** such as **Plasmapheresis (also known as Plasma Exchange or Pheresis or Apheresis)** and **Plasma Infusion**, Plasma therapy is the most traditional way to treat patients with aHUS. By transfusing FFP (Fresh Frozen Plasma) from a healthy donor into an aHUS patient in the process known as Plasma Infusion, its potential benefit is supplementing chemical compounds found deficient or absent in the patient's body. Plasma is the liquid component of the blood which transports the cells (red and white blood cells as well as platelets) and also carries various chemical compunds throughout the body. Plasma can be thought of as "the glue that holds the blood together and prevents the blood from shattering". Some aHUS cases do not respond to plasma infusion or patients can prove sensitive to adding the extra volume of fluid, so plasmaphersis is indicated for plasma therapy. A special pheresis machine is used to filter out all of the body's original plasma, replacing it with plasma from a healthy blood donor. In smaller aHUS patients, total blood volume is low and requires that the tubing of the pheresis machine be primed with a donor unit of packed red blood cells. Requiring surgery to place a 'central line' for plasmapheresis access, this process is more invasive but can also help to get control of the disease faster. Keeping the central line dry and sterile is of utmost importance. Patients with genetic mutations seem to respond especially well to plasma therapies.

***Soliris (generic name: Eculizumab)**

A recent development in aHUS treatment is a set of clinical trials being conducted by Alexion Pharmaceuticals, makers of Soliris. Soliris is an intravenous (IV) drug that is FDA approved to prevent hemolysis (red blood cell destruction) in adult patients with the rare disease PNH. Even though this drug has not completed clinical trials for aHUS patients and is not currently FDA approved for atypical hemolytic uremic syndrome, many aHUS patients are currently being treated very successfully with this medicine. Some aHUS patients are seeing long-term remission for the first time, as well as increased quality of life. Since maintaing kidney function is a major goal with aHUS patients, Soliris hold major potential to prevent further kidney damage as it interrupts the process of hemolysis by

disrupting the complement cascade. If given soon upon initial presentation/diagnosis of aHUS, Soliris potentially can prevent long-term damage to the kidneys - as noted in the Soliris Forum of this website. While currently an "off label" use and NOT yet FDA approved, Soliris use is an new option for doctors to discuss on a case by case basis.

Access Choices

Accessing a patient's veins for treatment can be one of the most stressful times for aHUS patients and their family. In order to treat the disease, doctors must have quality intravenous (IV) lines to use. There are a large variety of IV lines such and while the standard or common IV line familiar to most people, most often the frequency of aHUS treatments and lab work monitoring will require a longer-term solution such as a picc line or the longest term choices of 'central line' such as a port-a-cath (under the skin) or a broviack or tessio line (external, with a dressing that needs to be dry and sterile). No matter the type of bloodstream access, it is imperative that STERILE PROCEDURES are implemented each and every time the line is accessed or de-accessed. A line infection can be life-threatening. (See this site's Line Care Forum.) Plasma infusions can be done with the familiar vein prick and common IV line. This is the least invasive option but be aware that nursing staff will often be directed to 'pack' the line with Heparin to maintain a fully functional IV access for a period from hours to days. Keep an eye out for swelling, bruising, or site pain and notify medical staff at the appearance of any one of these warning signs. Other access choices will require a surgery to implant a device to allow longer term or specialized treatment access to the patient's blood stream. For example, plasmapheresis treatments remove (then discard) the aHUS patient's plasma from their blood and replace it with plasma from a healthy blood donor. This treatment requires a central line that has TWO lumens (end caps), one for blood flow out of the patient and the second to return blood flow back to the patient. Prior to the surgery, your doctor or nursing staff should be able to show you a "teaching board" display so that you can see the intended device pre-surgery and understand its benefit/need. Some doctors do have a preferred method/implant, but the access or line choice will be determined by the treatment needed as indicated by such lab values as CBC (complete blood cell count), LDH (a chemical marker of degree of aHUS activity), and CMP (complete metabolic panel).

Labs (Bloodwork)

Lab results can be confusing to those patients and family dealing with a newly diagnosed case of atypical HUS. Ask lots of questions! It is vitally important important that you understand the basic labs -you are the first in 'line of care' for your loved one and will often be called upon to give brief medical histories to medical personal. Treatment options and frequency (more treatments, spacing out treatments, moving from plasma infusions to plasmapheresis) are choices dependent on the trends seen

in the lab values. These are some of the most common labs ordered for aHUS patients - know whether the specific lab test is trending up or down from each lab draw to the next. (Keeping a log, diary, or paper copy of lab values is helpful to many aHUS patients and their families.) * **Hemoglobin, Hematocrit ('Crit)** - together comprising the 'H&H', and red blood cell count (RBC) all have to do with the ability of the patient's blood to carry oxygen throughout the body. Higher lab values are better - low numbers mean anemia that may result in a tired or lethargic set of patient behaviors. If the patient has a low red blood cell count (anemia is a common aHUS issue), doctors often will seek to promote increased red blood cell production with the drug erythropoietin aka 'epo' or a similar time-release drug called Aranesp. * **Platelets** are cell fragments that help in the clotting process. Low numbers may visually be displayed as the patient skin's may more easily bruised, so black and blue marks should be reported to the medical team. * **White blood cell counts (WBC)** High values can mean there is an infection. is a chemical marker of aHUS disease activity, so a high number or upward trend means that the aHUS espisode is getting worse ('ramping up') so treatment may need to be more aggressive. ***Haptoglobin** is another marker of hemolysis. When red blood cells break down, they release hemoglobin into the bloodstream. The hemoglobin combines with a chemical called haptoglobin. A low level of haptoglobin in the bloodstream is another indicator of active HUS. ***Creatinine** indicates kidney function and is a vital lab number to know with every set of lab tests. Lower is better, since creatinine indicates that toxins are effectively being eliminated from the body through the kidney's production of urine. High creatine levels mean that the kidneys are not functioning properly and that toxins can build up in the body to dangerous levels. In ESRD (end stage renal disease), the kidneys stop clearing toxins through urine so dialysis is needed to remove fatal levels of toxins from the patient's body. Protein in the urine is another measurement of kidney function, as poorly functioning kidneys spill out too much protein. ***Blood Urine Nitrogen (BUN)** indicates many factors including how well hydated the patient's body can maintain itself and so how the kidney function can keep normal body fluid levels. Numbers should trend lower here.

Common Kidney Lingo

Medical terms are often used as shorthand to describe the aHUS patient's condition or treatment plan, so be sure to ask when a term unknown to you crps up in conversation or on the medical history reports. Often, it will give you a heads up about whether the situation is improving, deteriorating, or remaining stable. Understanding the patient's blood work is essential to assessing the risk of kidney failure. ***CKD** - Chronic Kidney Disease - CKD is a progressive loss of kidney function over months or years and is often noted in 5 stages. Kidney function issues are detected/discussed using lab test values for creatinine and BUN (blood urea nitrogen), as well as the creatinine clearance rate and the eGFR (estimated glomerular filtration rate). ***The Renal Diet** - The renal or kidney diet helps patients reduce the amount of waste products produced which lessens the workload of the kidneys. It's important to note that there is NO single 'kidney diet" you can utilize from an on-line resource, as diets

are tailored to each patient's kidney function and overall health. Most kidney-friendly diets limit potassium, phosphorus, and sodium intake to varying degrees but the patient's doctor will often arrange a consult with nutritionists/dieticians to ensure a personalized dietary plan that works in conjunction with the aHUS patient's treaments and medications. ***ESRD** - End Stage Renal Disease - ESRD means that the kidneys can no longer effectively clear water and waste products from the body. By this point doctors will have outlined the mechanics of kidney failure with the aHUS patient/family and dialysis options and treatments are key discussion topics. ***Uremia**- As kidney function deteriorates and the body is less able to clear water/waste products, toxins can build up in the body causing uremia. Symptoms include: weakness, fatigue, nausea, vomiting, itching of the skin, muscle cramps, joint aches and pains, blurred vision, and sleep problems. ***Dialysis** - When a patient is in ESRD, discussions revolving around dialysis should occur in the event of renal failure. When kidney function fails, they can no longer perform their primary life-sustaining function of removing water and waste from the body. Diet, treatment center availabilty, family circumstances, and lifestyle are among the primary consideration when dialysis becomes necessary to artifically do the kidneys' job. Hemodialysis (blood stream access) aka 'hemo' and peritoneal dialysis (solution exchange in the abdomen) aka 'PD' both require access points made surgically. Both methods have their positive points and dialysis choice will vary according to the aHUS patient's situation and lifestyle choices.

Going Home - aHUS Follow Up Labs

Atypical HUS is characterized by repeated relaspses, which can be severe even though symptoms are slight. At initial diagnosis, aHUS patients will likely be hospitalized from weeks to months in order to get a handle on the disease. When the doctors feel you/your child is healthy enough, they will begin to train you in all aspects of home care and will set a care plan that includes follow-up appointments/lab work/ treatments. Due to the rarity of aHUS, few doctors are familiar with diease and its hallmarks of complexity, ferocity, and variability. Frequent labs can detect another episode and indicate the need for rapid treatment to attempt to protect kidney function during a relapse. Do not wait for distinct and pronounced symptoms, as often the only warnings will be a bit of patient tiredness, bruising, or perhaps vomiting. BE VERY PROACTIVE - ask for labs to be drawn at the first hint of any health or behavioral issues. Labs can often show aHUS activity BEFORE stymptoms occur .... do not wait for a follow-up or next scheduled appointment ! Every case is different, and no one can predict its course, so the most important goal is to treat aggressively to maintain the patient's kidney function.

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A Few Kidney-Related Links

While aHUS is a highly variable and complex rare disorder, you may wish to visit some of the websites below to obtain further information.

The National Kidney Foundation - http://www.kidney.org

The American Association of Kidney Patients - http://www.aakp.org

http://www.therenalnetwork.org and their secondary site http:kidneypatientnews.org which has important information and resources for patients and family members who want to learn more about CKD and dialysis.

Going to the ER

The Emergency Room (ER) staff typically does not have a lot of experience with HUS patients, especially atypical HUS. Before leaving the hospital after the initial diagnosis of aHUS, make sure you have an emergency plan in place as part of the aHUS patient's 'care plan'. Usually, most doctors treating aHUS patients will suggest that you CALL YOUR DOCTOR BEFORE HEADING TO YOUR HOSPITAL'S E.R. .Most doctors treating aHUS patients will have a 'direct admit' option, enabling you to skip the ER and be directly admitted to the floor that normally handles your aHUS treatments and associated care. ALWAYS bring you medications with you, since many are specialty medications and it often can take some time before the hospital pharmacy gets the drug ordered, filled, and up on the floor. NEVER give a medication without first checking with the patient's medical staff, as even regularly scheduled meds are sometimes switched due to current/urgent care needs. If you find yourself unexpectedly in the ER, give a full account of the last aHUS event, treatment, medications, and time spent in the hospital. Consider a 'grab and go' folder to bring along - with a letter from your doctor, a copy of recent labs, a list of medicines and their dosages, and other helpful details about your case.

Doctors Experienced with aHUS

As you browse through the Forums of this interactive website, you will see that the longer the battle with aHUS, the more complications that occur. Every attack can be potentially life threatening and repeated episodes of aHUS erode patient kidney function. Since this disease is rare, estimated to be about 300-600 cases in America, few doctors have seen or treated a single case of aHUS in their career. We recommend that you talk extensively with your doctors about all aspects of aHUS, referring them to both this site (our interactive site) and http://www.atypicalhus.50megs.com (our informational site). Our Home Page has a new "Doc to Doc Directory" so that your physicans can speak directly with colleagues who have offered to share their experiences with treatment of aHUS patients.

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Genetic Testing

When patients become stable, your doctors can find out additional information by sending blood samples for genetic testing to a specialized lab. In America, the primary genetic testing facility for aHUS patients is at the University of Iowa (see Links Box on our Home Page). Under the direction of Dr. Richard Smith, this lab currently does the most comprehensive genetic testing available for this disease. One or more of several different genetic abnormalities may be discovered through genetic testing, although about 50% of aHUS test results come back as being of unknown (ideopathic)

The Foundation for Children with Atypical HUS welcomes you into a supportive network of patients, family, friends, and researchers who truly care about the people dealing with the many medical and emotional issues facing aHUS families. We're here for you.....

Offered as an overview of aHUS to give you a base of knowledge as you begin your journey, the parents writing this article are NOT trained medical professionals, CONSULT YOUR DOCTOR for your case's details, since we have only covered a few basic areas and many things have not been included

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