Hemolytic Uremic Syndrome Handbook for Parents

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Your previously healthy child has suddenly become very unwell and has required hospital admission. Based on several tests, your doctor has informed you that your child's kidneys are failing because of "hemolytic uremic syndrome". Naturally you are worried and have many questions.

This booklet has been prepared to help answer the questions that you may have, including:

1. What is hemolytic uremic syndrome (HUS)?
2. Are there different types of HUS? What type does my child have?
3. What is the cause of HUS?
4. Can the illness happen in other family members?
5. What investigations are required?
6. What is the treatment?
7. How long will therapy last?
8. Is HUS curable and will kidney function return to normal?
9. Are dietary and other precautions necessary?
10. When and how should a doctor be consulted?

This booklet is designed to provide information that will guide you through your child's illness and teach how to provide adequate care at home.

Your doctors will be happy to discuss with you any matter regarding the illness.

What is hemolytic uremic syndrome?

Hemolytic uremic syndrome (HUS) is a rare disease. It is one of the most common cause of acute kidney failure in children requiring dialysis. HUS is caused by injury to the walls of small blood vessels. The injured blood vessel walls are sticky and form clots that interrupt the flow of blood to tissues. These tiny clots also trap red blood cells and platelets flowing though the vessels, damaging them in the process, leading to *hemolytic anemia* with broken red cells (*schistocytes*) and *thrombocytopenia* (low platelets). Vital organs, especially the kidneys, are injured by reduced blood flow (**Figure 1)**.

As a result, kidneys lose their ability to excrete waste products (e.g., urea, potassium) in urine, leading to their accumulation in the body, and symptoms such as nausea, vomiting, fatigue and, later, drowsiness or seizures. Blood vessel injury also causes high blood pressure. Other organs affected are the brain, heart, pancreas and liver.

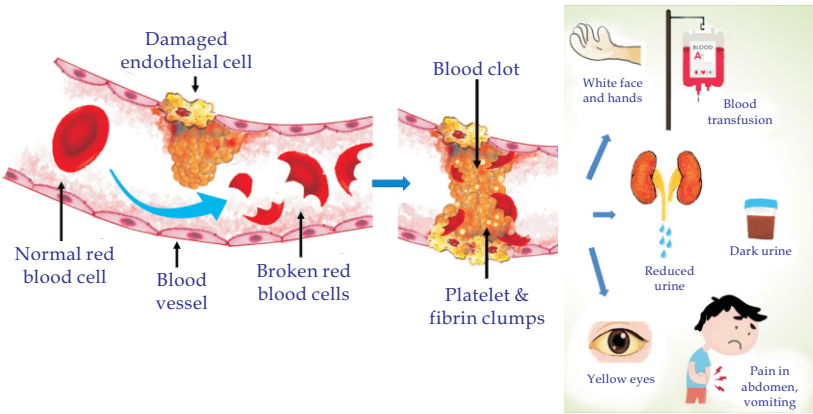

Figure 1: The figure shows various features of hemolytic uremic syndrome. The illness is caused due to injury to walls of small blood vessels causing blood clots, damaging red cells (schistocytes) and obstructing blood flow to organs, including the kidneys.

Untreated HUS is a progressive disease that causes permanent renal damage unless it is diagnosed and managed promptly. With appropriate management, hemoglobin and platelet count improve

and kidney function recovers. However, these patients may continue to require medications for high blood pressure. *All children should have regular clinic visits for several years, because there is risk of kidney damage that might be apparent later.*

HUS is a relapsing illness, which means that there is a risk for a similar episode in future. The kidney injury usually worsens with each relapse. *Parents must learn how to recognize a relapse early to prevent further damage to the kidneys.*

Types of HUS

HUS is of two main types: Shiga toxin associated and complement mediated (**Figure 2**). Shiga toxin associated HUS is caused by bacterial infection of the gastrointestinal tract either by *Escherichia coli* or *Shigella*. Complement associated HUS or atypical HUS is caused by dysfunction of complement proteins that normally protect the body's own cells and blood vessels from damage. Complement associated HUS occurs either due to mutations in essential genes or the presence of anti-factor H (FH) autoantibodies. Antibodies are substances produced by white cells to fight against infections. When antibodies react against cells of the own body, they are called autoantibodies.

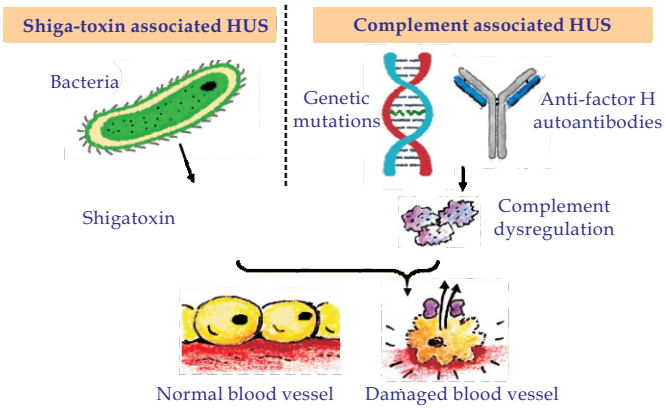

Figure 2: Types of hemolytic uremic syndrome. Shigatoxin associated HUS is caused by bacterial infection of the gastrointestinal tract. Complement associated HUS is either due to abnormalities in genes or formation of antibodies to complement factor H. Both diseases result in damage to endothelial cells lining the blood vessels.

Can the illness affect other family members?

Shiga toxin associated HUS is an infectious disease occurring through consumption of food contaminated with specific bacteria. Atypical HUS is not infectious and will not spread to others by food or close contact. Anti-FH antibody associated disease is not hereditary and does not occur in other siblings. However, the reason why antibodies develop is yet unknown.

Atypical HUS that is not associated with autoantibodies is hereditary and usually caused by a genetic mutation. The mutation can be inherited from the father, mother or both; other family members carry a 25-50% risk of disease. Before planning the next pregnancy, it is important to consult your doctor for prenatal diagnosis to know whether the unborn child is at risk.

What are the symptoms of HUS?

Symptoms often develops suddenly, over a span of a few days, and may follow an infection particularly of the upper respiratory tract or diarrhea. Children often complain of abdominal pain, vomiting, fatigue, lethargy or irritability. Parents may notice paleness of skin and lips, rash over arms or legs, swelling over face or legs, reduced passage of urine or red colored urine **(Figure 1).** Some children have been advised blood transfusion by doctors. High blood pressure is common and often severe. Symptoms are often severe enough to cause hospitalization.

What tests are required?

- Complete blood count, peripheral smear exam.
- Lactate dehydrogenase (LDH), haptoglobin.
- Urea, creatinine, sodium, potassium; liver function tests
- Complement C3
- Urine routine and microscopy
- Stool examination: culture, Shiga toxin
- Tests for hepatitis B and C; HIV

Specialized tests are antibody to complement factor H (FH), flow cytometry for membrane cofactor protein (CD46) and testing for complement genes.

Treatment

Most patients with Shiga toxin associated HUS require supportive care with attention to complications of renal failure, control of blood pressure and appropriate nutrition. Blood transfusions are required for severe anemia. The treatment of HUS associated with anti-FH antibodies or presumed complement defects is prompt plasma exchanges (PEX). Kidney injury may be mild and recover or severe enough to require dialysis. Once blood parameters and renal functions return to normal, the child is said to be in remission. *Normal activity and schooling should restart as soon as possible.*

What is plasma exchange (PEX)?

PEX is a procedure that removes and filters blood from the child to separate and discard 'plasma' containing harmful antibodies and complement proteins by passing it through a device called plasma filter. During this procedure of 1-2 hours, only small amount of blood is out of the body at any one time. Your child will be connected to the machine and can watch television, eat or drink during the procedure. Plasma that is removed is replaced by fresh frozen plasma (FFP) containing normal proteins. PEX does not hurt.

PEX has a small risk of allergic reactions like itching, rash, flushing, fever or a feeling of cold. There is a small risk of infections from the donated FFP, but blood products are carefully screened by the hospital blood bank. Very rarely, low blood pressure, breathlessness, cramps or seizures might occur. For more information, you may refer to the *PEX Reading Material* provided by your dialysis nurse.

What is a central venous catheter?

Both hemodialysis and PEX require a special catheter to access large blood vessels (veins) of the child as shown in **Figure 3**. The central venous catheter is inserted by trained doctors in the neck or groin. In order to ease pain, discomfort and anxiety during catheter insertion, your child is given medications before the procedure. They may have some local pain that wears off over a few hours.

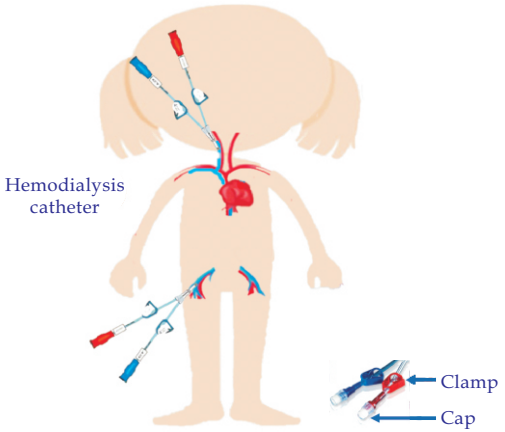

Figure 3: Site of central venous catheter for hemodialysis or plasma exchange is either the neck (jugular vein) or groin (femoral vein).

What is dialysis?

Dialysis is a temporary measure till kidneys recover from renal failure and start to make adequate amount of urine. Dialysis removes harmful substances that otherwise build up in the blood and make the child ill. This is possible by either peritoneal dialysis (though catheter inserted in the abdomen, **Figure 4**) or hemodialysis. Peritoneal dialysis is usually preferred in young children. It may be performed manually by the care provider or by an automated cycler, throughout the day for a few days. Hemodialysis cleanses the blood by passing it through a dialyzer attached to a dialysis machine. Hemodialysis is performed for four hours, three or more times per week, in the hospital.

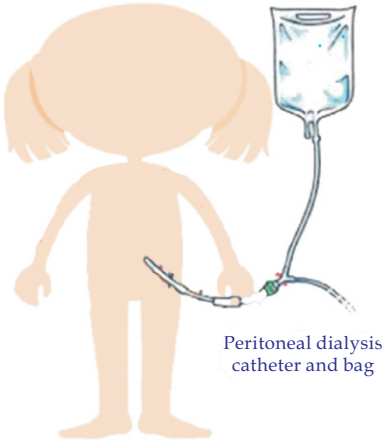

Figure 4: A special small catheter is inserted in the abdomen for peritoneal dialysis. This procedure is preferred in young children.

Dialysis may cause shift of fluid in the body that can lead to low blood pressure, cold hands and feet, muscle cramps, nausea or vomiting. Other problems include headache, chest pain or backache. Peritoneal dialysis may cause abdominal pain, discomfort and carry a risk of infection in the abdomen. Your doctor will monitor your child's vital signs (heart rate, blood pressure) during dialysis to detect any problems as quickly as possible.

Looking after the central venous catheter

It is important to maintain cleanliness around the catheter site. There is a risk of infection associated with central venous catheter. This may require IV antibiotics, replacement or removal of the catheter. If your child develops fever, contact your doctor urgently.

The following help to avoid problems associated with central venous catheters:

- Ensure that the catheter is taped securely to the skin and avoid getting it caught up in clothing. If the dressing comes off, a new dressing should be applied at home and the dialysis nurse informed at the next visit.

- The blood lines have caps that should never be removed. In case a cap comes off, do ensure that the clamp on that side is closed and the hospital is informed.
- Ensure the clamps on the blood lines are clamped at all times.
- If the catheter is inadvertently pulled, apply a tight dressing at the site and contact your doctor.
- If the catheter falls out, apply firm pressure for 10 minutes over the exit site until bleeding stops. If the bleeding gets worse or does not stop after 10 minutes, contact your doctor urgently. Once the bleeding has stopped, apply a dressing over the exit site.
- Contact your doctor if your child has fever (temperature >38^{0}C), if the exit site looks red or shows white or yellow discharge.

How soon can I take my child home after hemodialysis or PEX?

Dialysis and PEX are always done in the hospital. Once discharged from hospital, you may be required to come just for half a day. If there are no problems during the procedure, the child will be able to go home after a short rest.

Aditional Advice

Is there a limit on the amount of liquids my child can drink?

If child is passing less urine, your doctors will advise you to restrict fluids. If too much fluids are taken between dialysis sessions, the blood pressure goes up and the patient may become very unwell. No fluid restriction is necessary if the child is passing enough urine.

Does the child need a special diet?

Balanced nutrition is essential since an adequate diet helps in faster recovery. *You must give homemade energy-dense meals* like paranthas, ice cream, banana, sooji halwa, paneer, potato halwa, laddoos and gulab jamun. *The child also needs adequate protein* like chicken, fish, eggs, pulses, paneer and soyabean while on dialysis. Fruit juices should be avoided. A dietician will discuss and prescribe a diet to meet your child's needs.

Control of blood pressure

Extra-salt and food containing excessive salt (ketchup, pickles) must be avoided. Compliance with medications is essential to prevent further injury to kidneys, eyes and heart. Your doctor will usually advise you to buy a home blood pressure machine. Keeping a record of blood pressure measured at home, every morning and evening for 6-7 days before each OPD visit, will allow your doctor to titrate medications better.

Other medications

If your child has tested positive for anti-FH antibodies, medication is required to stop production of antibodies. *Prednisolone* (Wysolone, Omnacortil) is given as a single dose at 8 a.m. with milk. Monthly injection of IV *cyclophosphamide* (Endoxan) for 4-6 doses is given during day-care visits. This is followed by oral agents including *mycophenolate mofetil* (Cellcept, Mycept) or *azathioprine* (Azoran) for 1-2-years. While these medications are safe, complete blood count and liver function tests are required frequently.

If the patient is antibody negative, genetic testing is necessary to guide subsequent therapy. Certain genetic mutations require life-long therapy with infusion of FFP, every 7-10 days. The availability of eculizumab, a complement inhibitor, has significantly improved the outcomes of patients with complement associated HUS. Therapy needs to be administered at 2-3 weeks intervals for prolonged duration. This medication is expensive and currently not available in the country.

Infections and immunization

- Children receiving steroids (prednisolone), mycophenolate or azathioprine may become very ill if exposed to chicken pox or measles. *Contact your doctor at once, if your child has been exposed to chicken pox or measles.*
- Administration of live vaccines (e.g. against polio, measles-mumps-rubella, chicken pox) will be delayed until the child is off these medications.
- Your doctor will order tests to check if your child is immunized against hepatitis B.

What health problems can be expected in future?

HUS is a severe disease and the first episode or relapses may be life-threatening. Early diagnosis and prompt management significantly improves outcomes. Following recovery from acute illness, the child is at risk for hypertension and chronic kidney disease. *All children should have regular health check-ups every month in the initial few months and then every 3-4 months.* They require regular follow-up with a specialist, satisfactory control of blood pressure and an overall healthy life-style. Children who do not completely recover kidney function are at risk of end stage renal failure, chronic dialysis and kidney transplantation.

Early Recognition of Relapse

About 20% patents with HUS, particularly those not associated with Shiga toxin infection, are at risk of relapse of the disease. Relapses might occur at any time, but risk is greatest in the first 6-24 months of the illness. Relapse is usually preceded by a minor illness like cough, cold, fever or diarrhea. *Whenever the child has any of these infections, a complete blood count should be done.*

Early recognition of relapse is important. *Features that suggest a relapse include abdominal pain, nausea, vomiting, paleness of face or lips, slight yellowing of eyes, passing less urine, puffiness over eyes, brownish urine or general feeling of being unwell.* If the child has any of the above signs, your doctor should be consulted urgently.

Monitoring the urine for blood might enable early detection of relapses (**Figure 5**). The first morning urine specimen, is collected in a clean container. The reagent covered paper-strip is dipped in urine for a few seconds. Any change in color after a minute, is compared to the printed label on the bottle marked as "BLO".

Urine should be examined for blood every alternate day during infections, or if the child feels unwell; any change in color should be informed to your doctor.

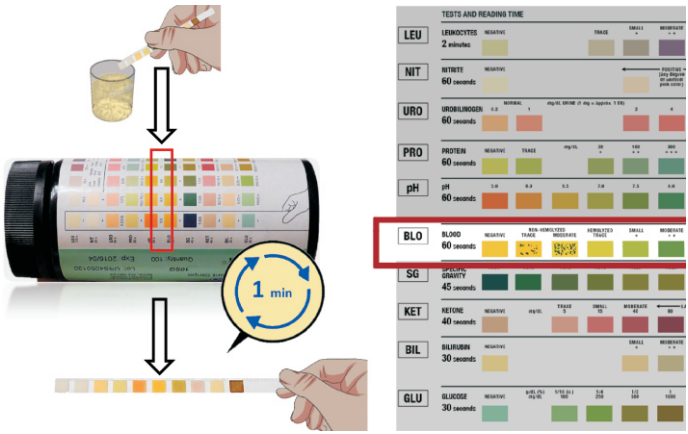

Figure 5: Urine dipstick examination at home for presence of blood. Collect the first morning urine specimen in a clean container and dip the reagent covered paper-strip in urine for a few seconds. After a minute, any change in color is compared to the printed label on the bottle marked as "BLO".

Responsibilities of parents and family?

- Parents must remember the signs of a relapse and consult a doctor immediately. Features suggesting relapse include abdominal pain, nausea, vomiting, paleness of face or lips, yellowing of eyes, passing less urine, puffiness over eyes, brownish urine or general feeling of being unwell.
- Test for complete blood count during infections to detect an early relapse
- Examine the urine by dipstick for blood every alternate day during infections or if the child feels unwell; consult your doctor if test is positive.
- Monitor blood pressure at home morning and evening for 6-7 days before each OPD visit. Consult your doctor for persistently high blood pressure recorded at home.
- Live vaccines must be avoided when the child is receiving steroids and other immunosuppressive medications.
- Consult a specialist doctor every month in the initial few months then every 3-4 months.
- Ensuring compliance to medication, especially medication to control blood pressure is important.

When and how should a doctor be consulted?

Apart from routine visits, urgent consultation with your doctor is required if the child has:

- Signs of relapse
- Urine examination at home during infections shows presence of blood
- Problems related to the central venous catheter: fever, bleeding or displacement.
- Severe headache or persistently high blood pressure
- Exposure to chicken-pox in children receiving prednisolone, mycophenolate or azathioprine

Please report punctually to the Dialysis Unit at the appointed time
7:30 a.m. for morning shift
1:30 p.m. for afternoon shift

You will be occasionally required to donate blood to the Blood Bank so that fresh frozen plasma may be obtained for plasma exchange

Contact details

Pediatric Hemodialysis (5th floor, D5 ward)	011-26546653
Pediatric Ward (5th floor, D5 ward)	011-26594753
Pediatric Emergency	011-26594225
Senior Resident Nephrology	9868397534

In case of any emergency, you must bring your child to the pediatric casualty.

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