

Hydroxyurea for Sickle Cell Disease



A Guide for Starting Treatment

Hydroxyurea is a medicine proven to prevent pain from sickle cell disease.

This handbook was created to help answer common questions about hydroxyurea treatment. If you have questions after reading this handbook, talk to your health care team.

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Children's National™

Hydroxyurea History

Is hydroxyurea a new medicine?

No. Hydroxyurea has been used as a medical treatment since 1869. It was first used to treat blood cancers. Doctors saw that hydroxyurea changed the hemoglobin inside red blood cells so they then studied it in people with sickle cell disease.

Hydroxyurea has been used to treat people with sickle cell disease for more than 30 years.

In the early 1990s, a study of adults with sickle cell disease that compared hydroxyurea to no treatment was ended early because hydroxyurea clearly decreased certain sickle cell problems. Adults treated with hydroxyurea had fewer pain crises, acute chest syndrome events, and transfusions. This study showed that hydroxyurea was helpful for adults, but more research was needed for children with sickle cell disease.

BABY HUG Study

In 2003 the BABY HUG study began to look at the safety and effectiveness of hydroxyurea in young children with sickle cell disease. **Infants treated at Children's National participated in the BABY HUG study.** This study included infants ages 9-18 months who had hemoglobin SS or S β^0 thalassemia. Some of the infants in this study had never had pain from sickle cell. The infants received either hydroxyurea or placebo (no medicine). These children were then followed for two years.

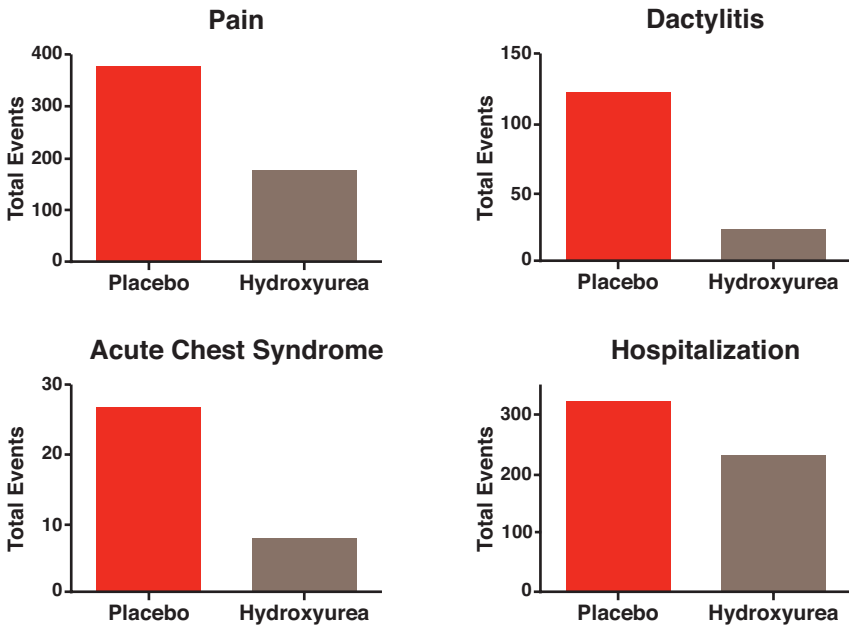
193 infants with Hemoglobin SS or S β^0

→ **96** hydroxyurea

→ **97** placebo
(no medicine)

BABY HUG Results

The BABY HUG study showed that hydroxyurea treatment was helpful and safe for children with sickle cell disease. Children treated with hydroxyurea had less pain, dactylitis (painful swelling of the hands or feet), acute chest syndrome, hospital visits, and transfusions. Hydroxyurea also improved transcranial Doppler (TCD) measurements.



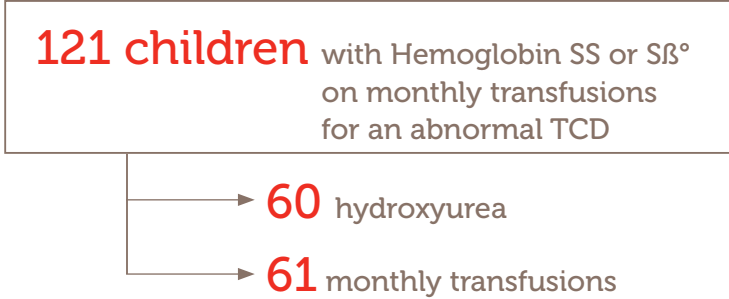
Thomberg, CD et al. Impact of hydroxyurea on clinical events in the BABY HUG trial. *Blood* 2012; 120(22):4304-4310

In this study hydroxyurea did not cause any serious side effects. Children treated with hydroxyurea did not have more infections. Children treated with hydroxyurea did not have more liver or kidney problems.

TWiTCH Study

Transcranial Doppler (TCD) ultrasound measures the flow of blood to the brain to determine if a child with sickle cell disease is at risk of stroke. Children who have an abnormal TCD measurement are at very high risk for having a stroke. Fortunately, the risk of stroke can be decreased by giving blood transfusions every month. Unfortunately, blood transfusions have serious side effects.

In the past, it was recommended that most children with an abnormal TCD should receive life-long blood transfusions every month to prevent stroke. The TWiTCH study asked if it was safe for these children to stop monthly transfusions after starting hydroxyurea. **Children treated at Children's National participated in this study.** The study included children on monthly transfusions for an abnormal TCD who did not have serious problems with their brain's blood vessels. The children either received hydroxyurea or continued monthly transfusions.



The results of this study were published in 2015. Children in the hydroxyurea group had similar TCD measurements to children in the monthly transfusion group.

In this study children treated with hydroxyurea did not have any strokes.

The TWiTCH study showed that hydroxyurea can substitute for monthly transfusions to prevent stroke in some children with sickle cell disease.

Long-term Use

Does hydroxyurea cause cancer?

No. Hydroxyurea does NOT cause cancer.

Unfortunately, children with sickle cell disease can get cancer. Fortunately, hydroxyurea does not increase the chances of a child with sickle cell disease getting cancer.

Is it safe to take hydroxyurea for many years?

We are still learning about the long-term effects of hydroxyurea, but many people with sickle cell disease have taken it safely for many years.

We recommend life-long treatment. Children treated with hydroxyurea grow and develop normally.

People with sickle cell disease unfortunately do not live as long as people who do not have sickle cell disease. Hydroxyurea may help change this.

People with sickle cell disease on hydroxyurea are living longer.



Not Just For Severe Disease

Who should take hydroxyurea?

In the past, doctors recommended hydroxyurea for patients with hemoglobin SS disease or $S\beta^0$ thalassemia who had frequent pain or recurrent acute chest syndrome. Today, we suggest hydroxyurea as a good option for most children with sickle cell disease, even children who have never had a pain crisis.

All children with hemoglobin SS and $S\beta^0$ should be offered hydroxyurea, according to National Institutes of Health guidelines.

Some children with hemoglobin SC and $S\beta^+$ thalassemia who have had pain crisis or acute chest syndrome may also benefit from hydroxyurea. Less is known about the use of hydroxyurea for these types of sickle cell disease.

One pain crisis is one too many.

We want to prevent sickle cell pain if possible. If your child has hemoglobin SS or $S\beta^0$ thalassemia, you don't need to wait for him or her to have pain to start hydroxyurea.

In addition to preventing pain, it may be helpful to start hydroxyurea early for other reasons. **Unfortunately, beginning in early childhood, sickle cell disease causes organ damage that likely will get worse over time.** Hydroxyurea may slow this damage. It is best to start hydroxyurea before sickle cell disease causes permanent damage.

We know from the BABY HUG study that we can safely start hydroxyurea in babies as young as 9 months.

“We are very fortunate that to this point we have never experienced a pain crisis, and we attribute this to the hydroxyurea and highly recommend the treatment.”

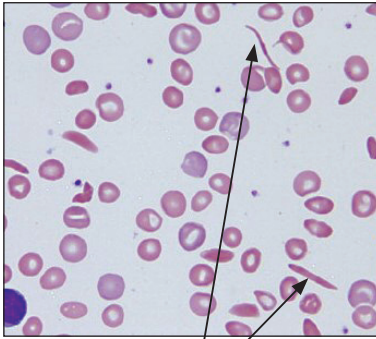
Red Blood Cell Changes

How does hydroxyurea work?

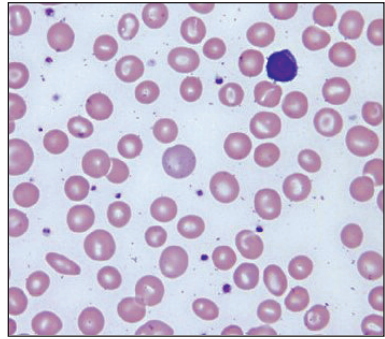
Hydroxyurea makes red blood cells bigger and less likely to sickle.

Newborns with sickle cell disease do not have pain from sickle cell disease. Newborns are protected because they make F hemoglobin (F is for fetal) which does not sickle. The amount of F hemoglobin decreases with age and is usually low by the time a baby turns one year old. Hydroxyurea treatment increases F hemoglobin. Hydroxyurea treatment also lowers inflammation and works in other ways to help people with sickle cell disease.

Before Hydroxyurea



After Hydroxyurea



sickle red blood cells

Adapted from Ware, RE. *Blood* 2010; 115(26):5306

“Hydroxyurea has helped me a lot since I have started taking it... Dealing with sickle cell, the pain can come at any time. But with hydroxyurea it can prevent pain crisis from spiking up often. So you can live a normal life. It helps out a lot. If you take it every day it will prevent pain from coming as well as letting you live a normal life. So you can have fun and do the things you want to.”

Blood Count Checks

Blood cell counts must be checked during hydroxyurea treatment. Changes seen in the blood cell counts with hydroxyurea treatment include:

Measurement	Hydroxyurea Effect
Hemoglobin (Hb) amount of protein in red blood cells	↑
Mean cell volume (MCV) size of red blood cells	↑
Absolute neutrophil count (ANC) number of a type of white blood cells	↓

When starting hydroxyurea, blood counts should be checked every month.

Neutrophils are a type of white blood cell that fight infections. They also may play a role in causing a pain crisis. People with sickle cell disease usually have a high number of neutrophils. Hydroxyurea treatment decreases the number of neutrophils. Hydroxyurea dose is increased if the absolute neutrophil count (ANC) stays high. After a patient has been on the same dose for at least two months, blood counts may be checked less often.

Sometimes children with sickle cell disease taking hydroxyurea develop a low reticulocyte (young red blood cell), neutrophil, or platelet count. If this happens, your doctor or nurse practitioner may stop hydroxyurea to allow the blood cell count to come up and then start treatment again.

If blood counts are monitored, hydroxyurea is very safe.

Side Effects

All medicines have possible side effects. Side effects of hydroxyurea are not common in children with sickle cell disease. Hydroxyurea is classified as a chemotherapy medicine, but hydroxyurea does not cause the severe nausea or hair loss commonly seen with other chemotherapy medicines.

Most children who take hydroxyurea have no bad side effects.

Darkening of the fingernail beds may occur with hydroxyurea treatment. Some children may also complain of mild stomach pain with hydroxyurea. **We recommend taking hydroxyurea at bedtime to help prevent this side effect.** Other side effects of hydroxyurea are very rare. If a patient has a bad side effect, then he or she can stop taking hydroxyurea.

For male patients:

Hydroxyurea treatment may affect a man's sperm so he cannot get a woman pregnant (male infertility). Unfortunately, men with sickle cell disease can also have problems with fertility due to their sickle cell disease. While hydroxyurea may affect male fertility, men with sickle cell disease taking hydroxyurea have fathered healthy babies.

For female patients:

Hydroxyurea has caused birth defects in studies of pregnant animals. However, women with sickle cell disease taking hydroxyurea have become pregnant and had healthy babies. **More research is needed to know if hydroxyurea is safe to take during pregnancy.**

At this time hydroxyurea is not recommended for men or women trying to have a baby or who are pregnant.

“Hydroxyurea played a major role in my child’s life. He has had no medical problems. He has never had any side effects. He is doing extremely well in school.”

Daily Medicine

Hydroxyurea comes as liquid and pills. The liquid is only made at special pharmacies. Your care team can help you get it. You may need to take a different number of pills on certain days.

The dose of hydroxyurea will change based on your child's weight and blood cell counts. **Hydroxyurea is taken once each day.** If your child is taking penicillin, your child should continue to take penicillin with hydroxyurea. It is safe to take hydroxyurea with most other medicines, but check with your doctor and pharmacy first.

What if I miss a dose?

Do not take extra hydroxyurea to make up for a missed dose. Just make sure not to miss any other doses. Call your doctor if you have questions.

Hydroxyurea will only work to prevent problems from sickle cell disease if it is taken every day.

Parents should oversee their child's hydroxyurea treatment. Teenagers may be able to take hydroxyurea by themselves, but also often need reminders to take their hydroxyurea every day. Here are some things to help with taking hydroxyurea:

- Calendar to mark off
- Pill box
- Cell phone alarm

Do not get discouraged if your child has a pain crisis or acute chest syndrome a few weeks after starting hydroxyurea. Hydroxyurea should not be stopped during a crisis. Hydroxyurea treatment takes time to improve the blood cell counts and prevent problems from sickle cell disease.

Hydroxyurea may take 3-6 months to help.

Hydroxyurea helps!

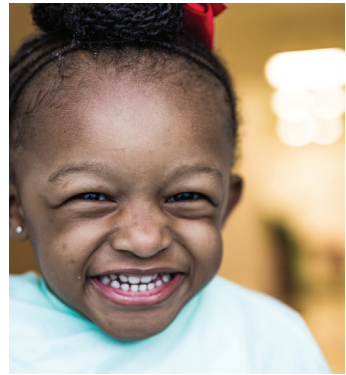
The quotes in this booklet were taken from Children's National patients and parents.

"As a parent I [would] like to advise other parents on the importance of hydroxyurea. For me, it really helped my daughter, who was always complaining about pain all day. Each time it was cool and most of winter, she [would] be hospitalized with a lot of pain. This is a good medication for those who want to try it."



"I am an advocate for hydroxyurea. When I meet people I tell them about hydroxyurea because it really has worked for my child."

"I'm thankful for hydroxyurea. It has been a positive experience. It has made a difference in my child's health from infancy and now he is 12 years old."



"Hydroxyurea has decreased my child's pain crisis and improved her quality of life."

"Hailing from a country with limited resources, my daughter fell ill numerous times. Even with our migration to the United States, she would still fall ill from time to time... Having her in the hospital so often because of her illness would be very emotional and heart wrenching... Fortunately, with the research that has been done, Children's National introduced the hydroxyurea drug to us. It has been a full year since my daughter has last seen a hospital room. She is able to run and jump freely and also has recently won a 100% attendance award from her school."



"Hydroxyurea has given me the opportunity to be able to take control of my body and focus on the other things in life. It gave me the chance to live life to the fullest even with Sickle Cell Anemia."



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