

# What is Hydroxyurea?

An overview of Hydroxyurea as treatment for Sickle Cell Disease

## Why use hydroxyurea?

Hydroxyurea is prescribed for patients with sickle cell disease to help reduce the frequency of pain episodes and acute chest syndrome. This includes adults and adolescents with moderate or severe recurrent pain.



## Who should be using hydroxyurea?

Anyone with:

- ◆ Frequent pain crises
- ◆ Acute chest syndrome
- ◆ Severe anemia
- ◆ Priapism, leg ulceration
- ◆ Presence of multiple allo-antibodies

## Who should *not* be using hydroxyurea?

- ◆ Pregnant or sexually active men and women not using contraception
- ◆ People with active liver disease

## What are the risks and side effects?

- ◆ Side effects are often predictable and will almost always go away after treatment is complete.
- ◆ There are many options to help decrease or prevent side effects.
- ◆ The side effects of Hydroxyurea and their severity depend on how much of the drug is given:
- ◆ **Common** (greater than 30% of patients):
  - Reduction of white blood cells (neutropenia) and clot-forming platelets (thrombocytopenia)
- ◆ **Less Common** (10-29% of patients):
  - Hair loss or thinning
  - Nausea and vomiting
  - Constipation or diarrhea
  - Mouth sores
  - Poor appetite
  - Nail thickening
  - Discoloration of the skin or nails
- ◆ **Rare** (less than 10% of patients):
  - Changes in fertility
  - Long-term use of hydroxyurea may increase the risk of developing leukemia, but the significance of this risk is not clear for those with sickle cell disease.

*For some patients, the risks of untreated sickle cell disease may outweigh the risks of hydroxyurea side effects.*



## Decreasing the risk of death

Hydroxyurea reduces the risk of serious complications with sickle cell disease, some of which can be deadly. One study concluded that over 9 years, there was a 40% reduction in death among people with sickle cell disease who used hydroxyurea.

PATIENTS MUST BE UNDER THE SUPERVISION OF A PHYSICIAN EXPERIENCED WITH THE DOSING AND MONITORING OF HYDROXYUREA

Charache S, Terrin ML, Moore RD, et al. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. Investigators of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia. *N Engl J Med*. May 18 1995;332(20):1317-1322.

Steinberg MH, Barton F, Castro O, et al. Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia: risks and benefits up to 9 years of treatment. *JAMA*. Apr 2 2003;289(13):1645-1651.

Monograph on the Potential Human Reproductive and Developmental Effects of Hydroxyurea. National Toxicology Program Center For The Evaluation of Risks To Human Reproduction October 2008 NIH Publication No. 08 – 5993

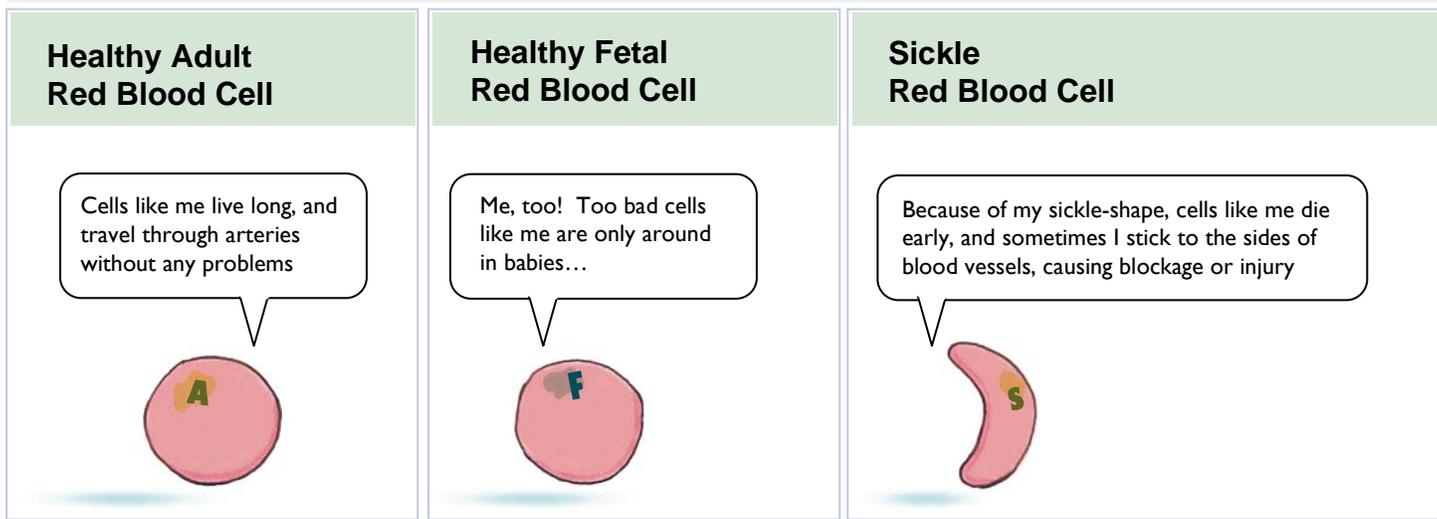
Segal JB, Strouse JJ, Beach MC, Haywood C, Witkop C, Park HS, Wilson RF, Bass EB, Lanzkron S. Hydroxyurea for the Treatment of Sickle Cell Disease. Evidence Report/Technology Assessment No. 165. (Prepared by Johns Hopkins University Evidence-based Practice Center under contract No. 290-02-0018). AHRQ Publication No. 08-E007. Rockville, MD. Agency for Healthcare Research and Quality. February 2008.



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# How do sickled blood cells affect your body?



Red Blood Cells with damaged Sickle Hemoglobin affect different people in different ways:

## 1 Deformed Shape

**Sickle red blood cells change shape, making them more likely to clog up blood vessels.**

*Result:* More frequent painful crises, acute chest syndrome, functional asplenia, acute stroke

## 2 Shorter Lifespan

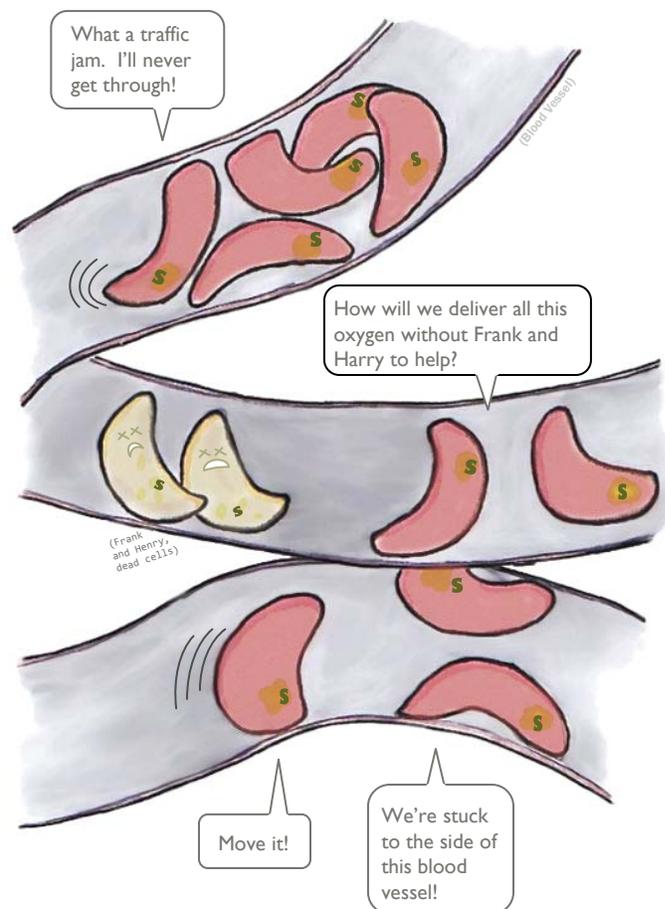
**Sickle red blood cells die off sooner than healthy red blood cells. As a result, the body has fewer red blood cells.**

*Result:* Less Nitric Oxide available, increased vascular tone, increased pulmonary-artery hypertension

## 3 Sticky Surface

**Sickle red blood cells have a sticky surface that makes them stick to the walls of blood vessels, causing injury or blockage**

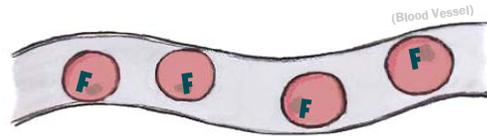
*Result:* More frequent vaso-occlusion, lesions, and inflammation from increased white blood cells and platelets



## What kind of red blood cells do you have?

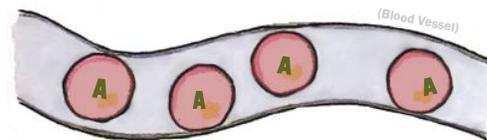
### Infant (Healthy or with Sickle Cell Disease)

Blood vessels of infants contain lots of red blood cells with Hemoglobin F (HbF) in them. These cells are round and healthy.



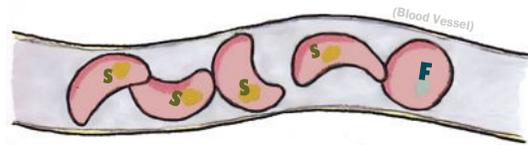
### Child or Adult (Healthy)

Blood vessels of healthy children or adults contain lots of red blood cells with Hemoglobin A (HbA) in them. A small number of red blood cells with fetal hemoglobin (HbF) may remain, but most go away with age.



### Child or Adult with Sickle Cell Disease

Blood vessels in people with sickle cell disease contain lots of red blood cells with sickle hemoglobin (HbS) in them. A small number of red blood cells with fetal hemoglobin (HbF) may remain.

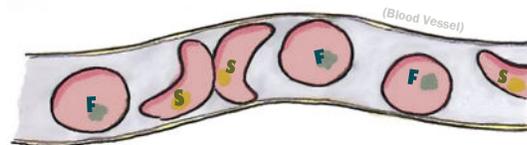


## How does Hydroxyurea treat Sickle Cell Disease?

Hydroxyurea reduces the severity of sickle cell disease by increasing production of fetal hemoglobin (HbF) and decreasing production of sickle hemoglobin (HbS). Hydroxyurea reduces the damaging effects of sickle cell disease, improves some aspects of quality of life, and may increase survival.\*

### Child or Adult with Sickle Cell Disease Using Hydroxyurea

Hydroxyurea causes more red blood cells with fetal hemoglobin to be made in the body. This reduces the proportion of the red blood cells with sickle hemoglobin (sickle cells).



\*A systematic review by a team from Johns Hopkins University concluded that mean percent of HbF prior to treatment ranged from 5 to 10 percent, compared to post-treatment values of 15 to 20 percent. They also determined that hydroxyurea therapy prevented the expected decline in percentage of HbF. Hemoglobin concentration increased slightly (1 gm/dl) but significantly across all studies examined.