

Sickle Cell News for February

Suspicious in the ER: a consequence of the opioid epidemic

<http://www.newsworks.org/index.php/local/item/100321-suspicious-in-the-er-an-unexpected-consequence-of-the-opioid-epidemic>

Diabetes drug metformin can help fight sickle cell disease, study shows

<https://knowridge.com/2017/01/diabetes-drug-metformin-can-help-fight-sickle-cell-disease-study-shows/>

Researchers at Baylor College of Medicine and Texas Children's Cancer and Hematology Centers have discovered a gene, *FOXO3*, involved in controlling fetal hemoglobin production.

In addition, the researchers were able to target the gene and "turn on" fetal hemoglobin levels in patient samples in the lab using the diabetes drug metformin.

This offers promising new treatments – the first new drug treatment for sickle cell disease in 30 years and the first ever for beta thalassemia.

"It was a major breakthrough to show that a common drug already in use for type 2 diabetes could be a treatment for sickle cell disease by inducing fetal hemoglobin, a type of hemoglobin that doesn't become sickle shaped but is usually turned off in infancy," said Dr. Vivien Sheehan, the lead investigator of the research.

Scientists aim to create the world's largest sickle cell disease stem cell library

<https://www.sciencedaily.com/releases/2017/01/170119134617.htm>

Scientists at the Center for Regenerative Medicine (CReM) at Boston Medical Center (BMC) and Boston University School of Medicine (BUSM) are creating an induced pluripotent stem cell (iPSC)-based research library that opens the door to invaluable sickle cell disease research and novel therapy development.

The library comprises blood samples from ethnically diverse patients with sickle cell disease from around the world and represents the major genetic backgrounds on which the sickle cell mutation occurred. The library is outlined in the current online issue of the journal *Stem Cell Reports*.

iPSCs are cells that can renew indefinitely as undifferentiated cells and later can be directed to grow into any type of tissue or organ. These stem cell lines can then be used to create disease models in a lab, which allows researchers to better understand how the disease occurs and develop and test new, effective treatments against the disease.

"Sickle cell disease affects millions of people worldwide and is an emerging global health burden," said George Murphy, PhD, co-founder of the CReM and assistant professor of medicine in the division of hematology-oncology at BUSM who is leading the project. "iPSCs have the potential to revolutionize the way we study human development, model life-threatening diseases, and eventually treat patients."

Sickle Cell Art and Black Art Puzzles for Black History Month by Artist Hertz Nazaire

Connecticut Commission on Equity and Opportunity presents: (énigme) Black Puzzle Series by artist Hertz Nazaire honoring Black History Month at Connecticut State Capitol lower level concourse. February 15th through 28th 2017 Connecticut State Capitol ,210 Capitol Avenue Hartford, Connecticut 06106 Open to the Public, Free NO TICKETS Needed :) but you can become a patron to support the Art creation process. <https://www.patreon.com/posts/enigme-black-7535351>

Hemoglobinopathy Counselor Training Course will be held on April 6-7, 2016. The two-day course, presented by the Cincinnati Comprehensive Sickle Cell Center, will be held at Cincinnati Children's Hospital Medical Center. The course registration fee is \$200. The deadline to register is March 24, 2017 and registration is limited. For more information, including a course brochure, please email:

SCDEvents@cchmc.org Registration is also available online at www.regonline.com/2017SCDCounselorcourse

African Sickle Cell News & World Report Oct-Dec 2016 Edition These and more available for free at [sickle cell news - hydroxyurea](#)

Articles in the medical literature

1. J Pediatr Hematol Oncol. 2017 Jan 17. doi: 10.1097/MPH.0000000000000783.

[Epub ahead of print]

[The Association of Serum 25-Hydroxyvitamin D With Biomarkers of Hemolysis in Pediatric Patients With Sickle Cell Disease.](#)

[Adegoke SA](#)¹, [Braga JA](#), [Adekile AD](#), [Figueiredo MS](#).

Abstract

Although vitamin D deficiency (VDD) has been linked to anemia among sickle cell disease (SCD), its relationship with hemolysis is unclear. Serum 25-hydroxyvitamin D and biomarkers of hemolysis (hemoglobin [Hb]/hematocrit, reticulocyte percentage, absolute reticulocyte, and lactate dehydrogenase [LDH] levels) in 36 hydroxyurea-naive SCD children were quantified. Correlations were significantly positive with Hb/hematocrit ($r=0.40$, $P=0.017$; $r=0.45$, $P=0.006$, respectively); inverse with reticulocyte percentage, absolute reticulocyte, and LDH ($r=-0.44$, $P=0.008$; $r=-0.47$, $P=0.007$; $r=-0.45$, $P=0.007$, respectively). In VDD groups, Hb was lower ($P=0.014$), reticulocyte counts and LDH were higher ($P=0.047$ and 0.003 , respectively). Serum

25-hydroxyvitamin D correlated with biomarkers of hemolysis in SCD and VDD may play a role in SCD pathogenesis.

PMID: 28099399 [PubMed - as supplied by publisher]

[Similar articles](#)

2. J Pediatr Hematol Oncol. 2017 Jan 17. doi: 10.1097/MPH.0000000000000743.

[Epub ahead of print]

[**Utilizing a Novel Mobile Health "Selfie" Application to Improve Compliance to Iron Chelation in Pediatric Patients Receiving Chronic Transfusions.**](#)

[Leonard S¹](#), [Anderson LM](#), [Jonassaint J](#), [Jonassaint C](#), [Shah N](#).

Abstract

Iron chelation therapy can prevent iron overload for pediatric patients with sickle cell disease and β -thalassemia major; however, adherence is suboptimal. Therefore, we developed an intensive training program (ITP), to improve medication management and disease knowledge. The objectives were to determine feasibility of the ITP and its preliminary impact on adherence, disease knowledge, and health outcomes. Pediatric patients were recruited to participate in the ITP over a 90-day period and were followed for 6 months. The ITP consisted of 3 components: (1) provider-led education modules; (2) patient recording daily videos of at-home medication administration; and (3) provider feedback through video messages through the ITP app. Eleven patients participated (mean=12.4 y). Initially, patients endorsed high satisfaction and ease of use and tracked their medication usage 81% (24 out of 30) of days. At 90 days, adherence rates remained consistent (80%) and disease knowledge retention was high (96%). At 6 months, participants exhibited a clinically relevant decrease in serum ferritin, which trended toward statistical significance ($P=0.068$). Medication possession ratio did not significantly increase (0.65 to 0.72; not significant). The mobile ITP was feasibly implemented in a clinical setting; in addition, high levels of compliance, disease knowledge retention, and acceptance encourage larger studies evaluating mobile health technology to improve child health parameters.

PMID: 28099398 [PubMed - as supplied by publisher]

[Similar articles](#)

3. JCI Insight. 2017 Jan 12;2(1):e89761. doi: 10.1172/jci.insight.89761.

[**Lung vaso-occlusion in sickle cell disease mediated by arteriolar neutrophil-platelet microemboli.**](#)

[Bennewitz MF](#)¹, [Jimenez MA](#)², [Vats R](#)², [Tutuncuoglu E](#)¹, [Jonassaint J](#)³, [Kato GJ](#)³, [Gladwin MT](#)⁴, [Sundd P](#)⁵.

Abstract

In patients with sickle cell disease (SCD), the polymerization of intraerythrocytic hemoglobin S promotes downstream vaso-occlusive events in the microvasculature. While vaso-occlusion is known to occur in the lung, often in the context of systemic vaso-occlusive crisis and the acute chest syndrome, the pathophysiological mechanisms that incite lung injury are unknown. We used intravital microscopy of the lung in transgenic humanized SCD mice to monitor acute vaso-occlusive events following an acute dose of systemic lipopolysaccharide sufficient to trigger events in SCD but not control mice. We observed cellular microembolism of precapillary pulmonary arteriolar bottlenecks by neutrophil-platelet aggregates. Blood from SCD patients was next studied under flow in an in vitro microfluidic system. Similar to the pulmonary circulation, circulating platelets nucleated around arrested neutrophils, translating to a greater number and duration of neutrophil-platelet interactions compared with normal human blood. Inhibition of platelet P-selectin with function-blocking antibody attenuated the neutrophil-platelet interactions in SCD patient blood in vitro and resolved pulmonary arteriole microembolism in SCD mice in vivo. These results establish the relevance of neutrophil-platelet aggregate formation in lung arterioles in promoting lung vaso-occlusion in SCD and highlight the therapeutic potential of targeting platelet adhesion molecules to prevent acute chest syndrome. PMID: 28097236 [PubMed - in process]

[Similar articles](#)

4. Proc Natl Acad Sci U S A. 2017 Jan 17. pii: 201619054. doi: 10.1073/pnas.1619054114. [Epub ahead of print]

[Kinetic assay shows that increasing red cell volume could be a treatment for sickle cell disease.](#)

[Li Q](#)¹, [Henry ER](#)¹, [Hofrichter J](#)¹, [Smith JF](#)¹, [Cellmer T](#)¹, [Dunkelberger EB](#)¹, [Metaferia BB](#)¹, [Jones-Straehle S](#)¹, [Boutom S](#)¹, [Christoph GW](#)¹, [Wakefield TH](#)², [Link ME](#)³, [Staton D](#)², [Vass ER](#)², [Miller JL](#)⁴, [Hsieh MM](#)⁵, [Tisdale JF](#)⁵, [Eaton WA](#)⁶.

Abstract

Although it has been known for more than 60 years that the cause of sickle cell disease is polymerization of a hemoglobin mutant, hydroxyurea is the only drug approved for treatment by the US Food and Drug Administration. This drug, however, is only partially successful, and the discovery of additional drugs that inhibit fiber formation has been hampered by the lack of a sensitive and quantitative cellular assay. Here, we describe such a method in a 96-well plate format that is based on laser-induced polymerization in sickle trait cells and robust, automated image analysis to detect the precise time at which fibers distort ("sickle") the cells. With this

kinetic method, we show that small increases in cell volume to reduce the hemoglobin concentration can result in therapeutic increases in the delay time prior to fiber formation. We also show that, of the two drugs (AES103 and GBT440) in clinical trials that inhibit polymerization by increasing oxygen affinity, one of them (GBT440) also inhibits sickling in the absence of oxygen by two additional mechanisms.

PMID: 28096387 [PubMed - as supplied by publisher]

[Similar articles](#)

5. Cochrane Database Syst Rev. 2017 Jan 17;1:CD003146. doi: 10.1002/14651858.CD003146.pub3. [Epub ahead of print]

[Blood transfusion for preventing primary and secondary stroke in people with sickle cell disease.](#)

[Estcourt LJ](#)¹, [Fortin PM](#)², [Hopewell S](#)³, [Trivella M](#)⁴, [Wang WC](#)⁵.

Abstract

BACKGROUND:

Sickle cell disease is one of the commonest severe monogenic disorders in the world, due to the inheritance of two abnormal haemoglobin (beta globin) genes. Sickle cell disease can cause severe pain, significant end-organ damage, pulmonary complications, and premature death. Stroke affects around 10% of children with sickle cell anaemia (HbSS). Chronic blood transfusions may reduce the risk of vaso-occlusion and stroke by diluting the proportion of sickled cells in the circulation. This is an update of a Cochrane Review first published in 2002, and last updated in 2013.

OBJECTIVES:

To assess risks and benefits of chronic blood transfusion regimens in people with sickle cell disease for primary and secondary stroke prevention (excluding silent cerebral infarcts).

SEARCH METHODS:

We searched for relevant trials in the Cochrane Library, MEDLINE (from 1946), Embase (from 1974), the Transfusion Evidence Library (from 1980), and ongoing trial databases; all searches current to 04 April 2016. We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Haemoglobinopathies Trials Register: 25 April 2016.

SELECTION CRITERIA:

Randomised controlled trials comparing red blood cell transfusions as prophylaxis for stroke in people with sickle cell disease to alternative or standard treatment. There were no restrictions by outcomes examined, language or publication status.

DATA COLLECTION AND ANALYSIS:

Two authors independently assessed trial eligibility and the risk of bias and extracted data.

MAIN RESULTS:

We included five trials (660 participants) published between 1998 and 2016. Four of these trials were terminated early. The vast majority of participants had the haemoglobin (Hb)SS form of sickle cell disease. Three trials compared regular red cell transfusions to standard care in primary prevention of stroke: two in children with no previous long-term transfusions; and one in children and adolescents on long-term transfusion. Two trials compared the drug hydroxyurea (hydroxycarbamide) and phlebotomy to long-term transfusions and iron chelation therapy: one in primary prevention (children); and one in secondary prevention (children and adolescents). The quality of the evidence was very low to moderate across different outcomes according to GRADE methodology. This was due to the trials being at a high risk of bias due to lack of blinding, indirectness and imprecise outcome estimates.

Red cell transfusions versus standard care

Children with no previous long-term transfusions

Long-term transfusions probably reduce the incidence of clinical stroke in children with a higher risk of stroke (abnormal transcranial doppler velocities or previous history of silent cerebral infarct), risk ratio 0.12 (95% confidence interval 0.03 to 0.49) (two trials, 326 participants), moderate quality evidence.

Long-term transfusions may:

- reduce the incidence of other sickle cell disease-related complications (acute chest syndrome, risk ratio 0.24 (95% confidence interval 0.12 to 0.48)) (two trials, 326 participants);
- increase quality of life (difference estimate -0.54, 95% confidence interval -0.92 to -0.17) (one trial, 166 participants);
- but make little or no difference to IQ scores (least square mean: 1.7, standard error 95% confidence interval -1.1 to 4.4) (one trial, 166 participants), low quality evidence.

We are very uncertain whether long-term transfusions:

- reduce the risk of transient ischaemic attacks, Peto odds ratio 0.13 (95% confidence interval 0.01 to 2.11) (two trials, 323 participants);
- have any effect on all-cause mortality, no deaths reported (two trials, 326 participants);
- or increase the risk of alloimmunisation, risk ratio 3.16 (95% confidence interval 0.18 to 57.17) (one trial, 121 participants), very low quality evidence.

Children and adolescents with previous long-term transfusions (one trial, 79 participants)

We are very uncertain whether continuing long-term transfusions reduces the incidence of:

- stroke, risk ratio 0.22 (95% confidence interval 0.01 to 4.35);
- or all-cause mortality, Peto odds ratio 8.00 (95% confidence interval 0.16 to 404.12), very low quality evidence.

Several review outcomes were only reported in one trial arm (sickle cell disease-related complications, alloimmunisation, transient ischaemic attacks). The trial did not report neurological impairment, or quality of life.

Hydroxyurea and phlebotomy versus red cell transfusions and chelation

Neither trial reported on neurological impairment, alloimmunisation, or quality of life.

Primary prevention, children (one trial, 121 participants)

Switching to hydroxyurea and phlebotomy may have little or no effect on liver iron concentrations, mean difference -1.80 mg Fe/g dry-weight liver (95% confidence interval -5.16 to 1.56), low quality evidence.

We are very uncertain whether switching to hydroxyurea and phlebotomy has any effect on:

- risk of stroke (no strokes);
- all-cause mortality (no deaths);
- transient ischaemic attacks, risk ratio 1.02 (95% confidence interval 0.21 to 4.84);
- or other sickle cell disease-related complications (acute chest syndrome, risk ratio 2.03 (95% confidence interval 0.39 to 10.69)), very low quality evidence.

Secondary prevention,

children and adolescents (one trial, 133 participants) Switching to hydroxyurea and phlebotomy may: increase the risk of sickle cell disease-related serious adverse events, risk ratio 3.10 (95% confidence interval 1.42 to 6.75); but have little or no effect on median liver iron concentrations (hydroxyurea, 17.3 mg Fe/g dry-weight liver (interquartile range 10.0 to 30.6)); transfusion 17.3 mg Fe/g dry-weight liver (interquartile range 8.8 to 30.7), low quality evidence. We are very uncertain whether switching to hydroxyurea and phlebotomy: increases the risk of stroke, risk ratio 14.78 (95% confidence interval 0.86 to 253.66); or has any effect on all-cause mortality, Peto odds ratio 0.98 (95% confidence interval 0.06 to 15.92); or transient ischaemic attacks, risk ratio 0.66 (95% confidence interval 0.25 to 1.74), very low quality evidence.

AUTHORS' CONCLUSIONS:

There is no evidence for managing adults, or children who do not have HbSS sickle cell disease. In children who are at higher risk of stroke and have not had previous long-term transfusions, there is moderate quality evidence that long-term red cell transfusions reduce the risk of stroke, and low quality evidence they also reduce the risk of other sickle cell disease-related complications. In primary and secondary prevention of stroke there is low quality evidence that switching to hydroxyurea with phlebotomy has little or no effect on the liver iron concentration. In secondary prevention of stroke there is low-quality evidence that switching to hydroxyurea with phlebotomy increases the risk of sickle cell disease-related events. All other evidence in this review is of very low quality.

PMID: 28094851 [PubMed - as supplied by publisher]

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7. Biol Blood Marrow Transplant. 2017 Jan 9. pii: S1083-8791(17)30077-0. doi: 10.1016/j.bbmt.2017.01.007. [Epub ahead of print]

[Enhanced Long-Term Brain MRI Evaluation of Children with Sickle Cell Disease Following Hematopoietic Cell Transplantation.](#)

[Green NS](#)¹, [Bhatia M](#)², [Griffith EY](#)³, [Qureshi M](#)², [Briamonte C](#)², [Savone M](#)², [Sands S](#)², [Lee MT](#)², [Lignelli A](#)⁴, [Brickman AM](#)³.

Abstract

Progressive neurovasculopathy in children with sickle cell disease (SCD) results in decreased cognitive function and quality of life (QoL). Hematopoietic cell transplant (HCT) is believed to halt progression of neurovasculopathy. Quantitative analysis of

T2-weighted fluid attenuated inversion recovery (FLAIR) MRI for white matter hyperintensity (WMH) burden provides a meaningful estimate of small vessel cerebrovascular disease. We asked if quantitative analysis of WMH could complement standardized clinical assessment of MRI/MRA for assessing SCD CNS vasculopathy pre- and post-HCT. Retrospective longitudinal clinical examination of scheduled annual MRI/MRA and quantitative analysis of WMH were performed 1-7 years pre- and post-HCT at scheduled annual intervals in engrafted children, along with QoL measurements. Of 18 patients alive and persistently engrafted (median age 9.1 years), pre-transplant MRI demonstrated that 9 and 5 had sickle-related stroke and/or small infarcts, respectively. Patients were divided into WMH severity tertiles based on pre-transplant WMH volumes. MRI and WMH were assessed 1-7 years post-HCT. MRI/MRA and WMH volume were stable or slightly better in 17 of 18 patients. By parent- and self-report, post-HCT QoL improved for children in the lowest WMH tertile significantly more than in the other groups. Based on this single-institution retrospective sample, we report that WMH appears to quantitatively support MRI-based findings that HCT stabilizes long-term small and large vessel cerebrovascular changes, and is associated with the degree of improved QoL. While confirmation in larger prospective studies and evaluation by neurocognitive testing are needed, these findings suggest that WMH is a useful biomarker of neurovasculopathy post-transplant for SCD.

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PMID: 28089760 [PubMed - as supplied by publisher]

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8. Sleep Breath. 2017 Jan 11. doi: 10.1007/s11325-017-1458-9. [Epub ahead of print]

[Hydroxyurea treatment effect on children with sickle cell disease and obstructive sleep apnea.](#)

[Grady AJ](#)¹, [Hankins JS](#)², [Haberman B](#)³, [Schoumacher R](#)³, [Stocks RM](#)⁴.

Abstract

BACKGROUND:

While hydroxyurea is the mainstay of treatment for many of the comorbidities associated with sickle cell disease, its effect on obstructive sleep apnea has not been fully investigated. The purpose of this project is to help characterize the effects of hydroxyurea on obstructive sleep apnea in children with sickle cell disease and determine its therapeutic role in the condition.

METHODS:

Chart review was conducted on two pediatric patients with sickle cell disease who experienced resolution of obstructive sleep apnea following hydroxyurea administration.

RESULTS:

After undergoing approximately 11 months of hydroxyurea therapy, sleep apnea symptoms improved and obstructive sleep apnea resolution was confirmed by repeat polysomnography in both cases. This resolution was largely secondary to a reduction in the obstructive component of the apnea hypopnea index, highlighting a previously unreported association.

CONCLUSIONS:

As adenotonsillectomy is associated with significant risks in patients with sickle cell disease, it appears reasonable to consider a period of observation for improvement of obstructive sleep apnea following hydroxyurea administration rather than directly proceeding with surgery.

PMID: 28078488 [PubMed - as supplied by publisher]

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10. Trans Am Clin Climatol Assoc. 2016;127:17-33.

[PRIMARY STROKE PREVENTION IN CHILDREN WITH SICKLE CELL ANEMIA LIVING IN AFRICA: THE FALSE CHOICE BETWEEN PATIENT-ORIENTED RESEARCH AND HUMANITARIAN SERVICE.](#)

[Debaun MR](#)¹, [Galadanci NA](#)¹, [Kassim AA](#)¹, [Jordan LC](#)¹, [Phillips S](#)¹, [Aliyu MH](#)¹.

Abstract

In the United States, primary stroke prevention in children with sickle cell anemia (SCA) is now the standard of care and includes annual transcranial Doppler ultrasound evaluation to detect elevated intracranial velocities; and for those at risk, monthly blood transfusion therapy for at least a year followed by the option of hydroxyurea therapy. This strategy has decreased stroke prevalence in children with SCA from approximately 11% to 1%. In Africa, where 80% of all children with SCA are born, no systematic approach exists for primary stroke prevention. The two main challenges for primary stroke prevention in children with SCA in Africa include: 1) identifying an alternative to blood transfusion therapy, because safe monthly blood transfusion therapy is not feasible; and 2) assembling a health care team to implement and expand this effort. We will emphasize early triumphs and challenges to decreasing the incidence of strokes in African children with SCA.

PMCID: PMC5216496 **Free PMC Article**

PMID: 28066035 [PubMed - in process]

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11. Biol Blood Marrow Transplant. 2017 Jan 5. pii: S1083-8791(17)30079-4. doi: 10.1016/j.bbmt.2017.01.009. [Epub ahead of print]

[Current Results and Future Research Priorities in Late Effects after Hematopoietic Stem Cell Transplantation \(HCT\) for Children with Sickle Cell Disease and Thalassemia: a Consensus Statement From the Second Pediatric Blood and Marrow Transplant Consortium International Conference on Late Effects after Pediatric HCT.](#)

[Shenoy S](#)¹, [Angelucci E](#)², [Arnold SD](#)³, [Baker KS](#)⁴, [Bhatia M](#)⁵, [Bresters D](#)⁶, [Dietz AC](#)⁷, [De La Fuente J](#)⁸, [Duncan C](#)⁹, [Gaziev J](#)¹⁰, [King AA](#)¹¹, [Pulsipher MA](#)⁷, [Smith A](#)¹², [Walters MC](#)¹³.

Abstract

Sustained donor engraftment after allogeneic hematopoietic cell transplantation (HCT) converts to healthy donor hemoglobin synthesis and halts disease symptoms in patients with sickle cell disease (SCD) and thalassemia major. A disease free survival probability that exceeds 90% has been reported when HCT using an HLA-matched sibling donor is performed in young patients with low risk disease or treatment related risk factors. Alternate donor HCT and HCT in adults is performed infrequently due to a higher risk profile. Transplant specific risks include conditioning regimen-related toxicity, graft-versus-host disease, graft rejection with marrow aplasia or disease recurrence, and infections associated with immunosuppression and delayed immune reconstitution. The magnitude of risk depends on patient age, clinical status of the underlying disease (e.g., organ injury from vasculopathy and iron overload), donor source, and intensity of the conditioning regimen. These risks are commonly monitored and reported in the short term. Documenting very late outcomes is important, but these data are rarely reported due to challenges imposed by patient drop-out and insufficient resources. This report summarizes long-term follow up results after HCT for hemoglobin disorders, identifies gaps in knowledge, and discusses opportunities for future investigations. This consensus summary will be followed by a second manuscript detailing comprehensive long-term follow up recommendations that will aid in maintaining health in these individuals and identifying late complication risks that could facilitate interventions to improve outcomes.

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12. J Pain. 2017 Jan 5. pii: S1526-5900(16)30375-3. doi: 10.1016/j.jpain.2016.12.016.
[Epub ahead of print]

[**AAPT Diagnostic Criteria for Chronic Sickle Cell Disease Pain.**](#)

[Dampier C, Palermo TM, Darbari DS, Hassell K, Smith W, Zempsky W.](#)

Abstract

Pain in sickle cell disease (SCD) is associated with increased morbidity, mortality, and high healthcare costs. While episodic acute pain is the hallmark of this disorder, there is an increasing awareness that chronic pain is part of the pain experience of many older adolescents and adults. A common set of criteria for classifying chronic pain associated with SCD would enhance SCD pain research efforts in epidemiology, pain mechanisms, and clinical trials of pain management interventions, and ultimately improve clinical assessment and management. As part of the collaborative effort between the Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks (ACTTION) public-private partnership with the U.S. Food and Drug Administration and the American Pain Society (APS), the ACTTION-APS Pain Taxonomy (AAPT) initiative developed the outline of an optimal diagnostic system for chronic pain conditions. Subsequently, a working group of experts in sickle cell disease pain was convened to generate core diagnostic criteria for chronic pain associated with SCD. The working group synthesized available literature to provide evidence for the dimensions of this disease-specific pain taxonomy. A single pain condition labeled Chronic SCD Pain was derived with 3 modifiers reflecting different clinical features. Future systematic research is needed to evaluate the feasibility, validity, and reliability of these criteria.

PERSPECTIVE:

An evidence-based classification system for Chronic Sickle Cell Disease (SCD) Pain was constructed for the AAPT initiative. Applying this taxonomy may improve assessment and management of SCD pain and accelerate research on epidemiology, mechanisms, and treatments for Chronic SCD Pain.

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13. Am J Med. 2017 Jan 5. pii: S0002-9343(16)31310-9. doi:
10.1016/j.amjmed.2016.12.010. [Epub ahead of print]

[**Risk Factors for 30-day Readmission in Adults with Sickle-Cell Disease.**](#)

[Brodsky MA¹, Rodeghier M², Sanger M³, Byrd J³, McClain B³, Covert B³, Roberts DO³, Wilkerson K³, DeBaun MR³, Kassim AA⁴.](#)

Abstract

BACKGROUND:

Readmission to the hospital within 30-days is a measure of quality care; however, only few modifiable risk factors for 30-day readmission in adults with sickle cell disease are known.

METHODS:

We performed a retrospective review of the medical records of adults with sickle cell disease at a tertiary care center, to identify potentially modifiable risk factors for 30-day re-admission due to vaso-occlusive pain episodes. A total of 88 patients > 18 years of age were followed for 3.5 years between 2010 and 2013, for 158 first admissions for vaso-occlusive pain episodes. Of these, those subsequently readmitted (cases) or not readmitted (controls) within 30 days of their index admissions were identified. Seven risk factors were included in a multivariable model to predict re-admission: age, gender, hemoglobin phenotype, median oxygen saturation level, listing of primary care provider, type of health insurance and number of hospitalized vaso-occlusive pain episodes in the prior year.

RESULTS:

Mean age at admission was 31.7 (18-59); median time to readmission was 11 days (IQR 20 days). Absence of a primary care provider listed in the electronic medical record (OR 0.38, 95% CI 0.16-0.91; $p = 0.030$) and the number of vaso-occlusive pain episodes requiring hospitalization in the prior year were significant risk factors for 30-day readmission (OR 1.30, 95% CI 1.16-1.44; $p < 0.001$).

CONCLUSION:

Improved discharge planning and ensuring access to a primary care provider may decrease the 30-day readmission rate in adults with sickle cell disease.

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PMID: 28065771 [PubMed - as supplied by publisher]

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14. J Pediatr Hematol Oncol. 2017 Jan 5. doi: 10.1097/MPH.0000000000000747.

[Epub ahead of print]

The Sickle β -Thalassemia Phenotype.

[Adekile AD](#)¹, [Akbulut N](#), [Azab AF](#), [Al-Sharida S](#), [Thomas D](#).

Abstract

S β -thalassemia (S β -thal) is common among Gulf Arab patients with sickle cell disease, but the phenotype of this group had not been well-documented. We have studied a group of Kuwaiti patients and compared the phenotype in the homozygotes (SS) and S β -thal patients. Complete blood count, hemoglobin quantitation, serum bilirubin, and lactate dehydrogenase were determined with standard techniques. The patients were screened for α -globin genotype. The S β -thal patients were also screened for the HBG2 Xmn-1 polymorphism. β -Thal mutations were determined by arrayed primer extension or direct sequencing. There were 70 SS and 32 S β -thal patients with mean ages of 14.8 \pm 5.9 and 14.2 \pm 5.9

years, respectively. The S β -thal patients had more frequent, severe pain episodes per year compared with the SS, while the patterns among S β -thal and S β -thal patients were not significantly different. There were no differences in the frequencies of acute chest syndrome, gallstones, and blood transfusion in the SS and S β -thal patients. However, none of the S β -thal patients had been transfused. Among the S β -thal patients, 25 had β -thal and 7 had β -thal mutations, the most common being cd39 (C \rightarrow T) and IVS-I-110 (G \rightarrow A), respectively. S β -thal shows a severe phenotype in Kuwait, even among those with S β -thal, in whom the IVS-I-110 (G \rightarrow A) mutation is predominant.

PMID: 28060121 [PubMed - as supplied by publisher]

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15. *Pediatr Blood Cancer*. 2016 Dec 30. doi: 10.1002/pbc.26401. [Epub ahead of print] **[Secondary benefit of maintaining normal transcranial Doppler velocities when using hydroxyurea for prevention of severe sickle cell anemia.](#)**

[Ghafuri DL](#)¹, [Chaturvedi S](#)², [Rodeghier M](#)³, [Stimpson SJ](#)⁴, [McClain B](#)⁴, [Byrd J](#)⁴, [DeBaun MR](#)⁴.

Abstract

In a retrospective cohort study, we tested the hypothesis that when prescribing hydroxyurea (HU) to children with sickle cell anemia (SCA) to prevent vaso-occlusive events, there will be a secondary benefit of maintaining low transcranial Doppler (TCD) velocity, measured by imaging technique (TCDi). HU was prescribed for 90.9% (110 of 120) of children with SCA \geq 5 years of age and followed for a median of 4.4 years, with 70% (n = 77) receiving at least one TCDi evaluation after starting HU. No child prescribed HU had a conditional or abnormal TCDi measurement. HU initiation for disease severity prevention decreases the prevalence of abnormal TCDi velocities.

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16. *Acad Emerg Med*. 2016 Dec 23. doi: 10.1111/acem.13154. [Epub ahead of print] **[Hot Off the Press: Which Febrile Children With Sickle Cell Disease Need a Chest X-Ray?](#)**

[Morgenstern J](#)¹, [Heitz C](#)², [Milne WK](#)³.

Abstract

This retrospective chart review examined the rate of acute chest syndrome (ACS) in febrile children (aged 3 months to 21 years) with sickle cell disease and used recursive partitioning to determine which clinical factors were predictive of a diagnosis of ACS. Over the course of 2 years, 697 children made 1837 visits to one of two pediatric emergency departments. ACS was diagnosed in 185 (10%) of the visits. This article is protected by copyright. All rights reserved.
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17. Cochrane Database Syst Rev. 2016 Dec 22;12:CD010378. doi: 10.1002/14651858.CD010378.pub3.

[Prophylactic versus selective blood transfusion for sickle cell disease in pregnancy.](#)

[Okusanya BO](#)¹, [Oladapo OT](#)².

Update of

- [Prophylactic versus selective blood transfusion for sickle cell disease in pregnancy.](#) [Cochrane Database Syst Rev. 2013]

Abstract

BACKGROUND:

Pregnant women with sickle cell disease (HbSS, HbSC and HbS β Thal) may require blood transfusion to prevent severe anaemia or to manage potential medical complications. Preventive blood transfusion in the absence of complications starting from the early weeks of pregnancy or blood transfusion only for medical or obstetric indications have been used as management policies. There is currently no consensus on the blood transfusion policy that guarantees optimal clinical benefits with minimal risks for such women and their babies. This is an update of a Cochrane review that was published in 2013.

OBJECTIVES:

To assess the benefits and harms of a policy of prophylactic versus selective blood transfusion in pregnant women with sickle cell disease.

SEARCH METHODS:

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 May 2016) and reference lists of retrieved studies. We did not apply any language or date restrictions.

SELECTION CRITERIA:

Randomised controlled trials evaluating the effects of prophylactic versus selective (emergency) blood transfusion in pregnant women with sickle cell disease (SCD). Quasi-randomised trials and trials using a cluster-randomised design were eligible for inclusion but none were identified.

DATA COLLECTION AND ANALYSIS:

Two review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. Two review authors independently assessed the quality of the evidence using the GRADE approach.

MAIN RESULTS:

Out of six relevant reports identified by the search strategy, one trial involving 72 women with sickle cell anaemia (HbSS) met our inclusion criteria. The trial was at unclear risk of bias. Overall, there were few events for most of the reported outcomes and the results were generally imprecise. The included trial reported no maternal mortality occurring in women who received either prophylactic or selective blood transfusion. Very low-quality evidence indicated no clear differences in maternal mortality, perinatal mortality (risk ratio (RR) 2.85, 95% confidence interval (CI) 0.61 to 13.22; very low-quality evidence) or markers of severe maternal morbidity (pulmonary embolism (no events); congestive cardiac failure (RR 1.00, 95% CI 0.07 to 15.38; very low-quality evidence); acute chest syndrome (RR 0.67, 95% CI 0.12 to 3.75)) between the treatment groups (prophylactic blood transfusion versus selective blood transfusion). Low-quality evidence indicated that prophylactic blood transfusion reduced the risk of pain crisis compared with selective blood transfusion (RR 0.28, 95% CI 0.12 to 0.67, one trial, 72 women; low-quality evidence), and no differences in the occurrence of acute splenic sequestration (RR 0.33, 95% CI 0.01 to 7.92; low-quality evidence), haemolytic crises (RR 0.33, 95% CI 0.04 to 3.06) or delayed blood transfusion reaction (RR 2.00, 95% CI 0.54 to 7.39; very low-quality evidence) between the comparison groups. Other relevant maternal outcomes pre-specified for this review such as cumulative duration of hospital stay, postpartum haemorrhage and iron overload, and infant outcomes, admission to neonatal intensive care unit (NICU) and haemolytic disease of the newborn, were not reported by the trial.

AUTHORS' CONCLUSIONS:

Evidence from one small trial of very low quality suggests that prophylactic blood transfusion to pregnant women with sickle cell anaemia (HbSS) confers no clear clinical benefits when compared with selective transfusion. Currently, there is no evidence from randomised or quasi-randomised trials to provide reliable advice on the optimal blood transfusion policy for women with other variants of sickle cell disease (i.e. HbSC and HbS β Thal). The available data and quality of evidence on this subject are insufficient to advocate for a change in existing clinical practice and policy.

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Sickle Cell Conferences and Events

Foundation for Sickle Cell Disease Research Annual meeting

April 28 -30 2017 Ft Lauderdale FL <http://fscdr.org/the-symposium/>

Hemoglobinopathy Counselor Training Course will be held on April 6-7, 2016. The two-day course, presented by the Cincinnati Comprehensive Sickle Cell Center, will be held at Cincinnati Children's Hospital Medical Center. The course registration fee is \$200. The deadline to register is March 24, 2017 and registration is limited. For more information, including a course brochure, please email:

SCDEvents@cchmc.org Registration is also available online at www.regonline.com/2017SCDCounselorcourse