Perspectives in Care for Children with Special Health Care Needs

FALL 2012

MD INSIGHTS

Features

LA RABIDA CHILDREN'S HOSPITAL

Perspectives in Care for Children with Special Health Care Needs

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About La Rabida

La Rabida is a pediatric acute care specialty hospital. The only hospital of its kind in Chicago, it treats children with chronic illness and disabilities. Its 49-bed inpatient unit is staffed and equipped to treat and manage:

- Medical technology dependency
- Recovery and rehabilitation following surgery, a NICU or PICU stay
- Acute exacerbations of a chronic illness
- Conditioning in preparation for medical procedures

La Rabida extends its interdisciplinary team approach to all outpatient care, offering a wide range of primary care programs and specialty clinics on site. In addition, the hospital provides psychosocial care for children who have experienced abuse, neglect and/or trauma.
La Rabida strives to be the hospital of choice and a trusted partner in the medical management of the children it serves and their families.

Medical Home Programs

- Adolescent
- Bronchopulmonary dysplasia
- Medically Complex Kids and Youth
- Failure to thrive
- Premier Kids (birth to age 5)
- NICU follow-up

Specialty Clinics

- Asthma, allergy
- Diabetes
- Down syndrome
- G-tube*
- Nephrology*
- Neurology*
- Orthopedics*
- Pediatric incontinence
- Physical medicine /rehabilitation
- Podiatry*
- Psychiatry*
- Rheumatology
- Sickle Cell
- Spasticity multispecialty management
- Traumatic brain injury

**For La Rabida patients only; unable to accept direct referrals.*

Spotlight

Medically Complex Kids and Youth: A Medical Home

The Medically Complex Kids and Youth (MCKY) clinic offers primary care for children and youth who have medically complex conditions and disabilities. Children appropriate for the clinic may include those with physical disabilities, genetic disorders, nutrition issues, risk factors from prematurity, or other chronic conditions. Children in the clinic will receive routine check-ups, immunizations and urgent care. Access to specialists and coordination of care are also key components to the clinic. La Rabida is recognized by the National Commitee for Quality Assurance (NCQA) for its medical home programs.

To refer a child, please call 773.753.8627

MD to MD

According to the latest statistics from the Centers for Disease Control, sickle cell disease currently affects 90,000 to 100,000 Americans, with a staggering proportion shouldered by African-Americans, where one in 500 have the full sickle cell disease, and one in 12 carry the sickle cell trait.

These are sobering numbers, and yet, thanks to a multitude of initiatives in the realms of early diagnosis, aggressive management, multidisciplinary preventive programs and ongoing research, tremendous progress has been made. This resulted in a 42 percent drop in sickle cell-related mortality among African-American children younger than four years of age between the year 1999 and 2002.

La Rabida Children's Hospital, in close partnership with the University of Chicago Medicine, has developed a state-of-the-art sickle cell program currently serving over 400 patients. This program is led by John M. Cunningham, MD, a highly respected authority in the field of sickle cell disease, with the expert support of Radhika Peddinti, MD, and Yasmin Abdullah, APN.

In this issue, our dedicated team provides us with comprehensive articles on the current state of sickle cell disease screening, pain management challenges, and therapeutic options. Articles also stress the all essential early detection and establishment of individualized management plans in order to minimize the potential future complications of sickle cell disease and maximize quality of life.

Furthermore, Patricia Engebretson, APN, and Cunningham present us with an overview of stem cell transplantation as a potential cure for sickle cell disease, discussing along the way patient selection criteria as well as ongoing and future research direction on the path towards the total eradication of this potentially devastating disease.

But no matter the achievements of the La Rabida sickle cell program, meaningful results cannot be sustained without the dedication and support of the community primary care physicians who remain on the frontlines of care and provide the basis of the all important Medical Home concept crucial to our sickle cell population.

Walid Maalouli, M.D., FAAP
Chief Medical Officer
La Rabida Children's Hospital

INSIDEINSIGHTS

Table of Contents

Walid Maalouli, M.D., FAAP, is La Rabida's Children's Hospital's first chief medical officer. He brings to the position more than 18 years of clinical and leadership experience in pediatric and hospital practice, most recently as founder and medical director of the hospitalist division at Children's Hospitals and Clinics of Minnesota, a tertiary care, multicampus provider.

Pain and Sickle Cell Disease: Challenges and Opportunities

John M. Cunningham, M.D., Yasmin Abdullah, A.P.N., and Radhika Peddinti, M.D.

The pain unique to the child with sickle cell disease (SCD) has been recognized for centuries. African tribes either use sound imitations to describe the crying unique to the toddler with SCD, or give it distinctive names such as 'hemkon' which is translated loosely as 'body biting.' Today, the acute painful crisis remains one of the greatest challenges to the child, parent and clinician. It is the most frequent cause for a visit to the emergency room, an admission to the hospital, and is of constant concern to the child and his/her parents.

Prevention and treatment of SCD-related pain continues to be an enigma to those physicians and other clinical staff either who do not care for children with SCD regularly, or are not appropriately trained in the biology, causes, complications, treatment and amelioration of the crisis and its sequelae. Not only is it important to understand these concepts to ensure that the acute episode is terminated rapidly and effectively, but the pathophysiologic consequences of a painful crisis guides appropriate therapeutic interventions that limit the chronic damage associated with repetitive tissue infarction.

"A careful history and physical can help decide whether to treat this yourself or refer"

Sickle hemoglobin, the result of a single amino acid change in the beta globin chain, polymerizes with hypoxia, dehydration, and the acidosis associated with infections or trauma. Inflexible sickle red blood cells damage the vascular endothelium, and form a vaso-occlusive plug with resultant hypoxia and tissue infarction or death. Children with a high hematocrit, neutrophil and/or platelet count experience an increased rate of crisis, fueling an inflammatory reaction that requires correction of the underlying precipitant for resolution.

Painful events are a continuous challenge to the patient with SCD, but are not limited to periods when the child presents to the parent or physician. Most children experience pain at some time during each day. However, a formal definition of a SCD pain crisis is pain in the back, abdomen, limb, chest, or head that lasts more than two hours. In children, 0.5 to one painful crises are observed per year, the rate increasing with age. However, great heterogeneity is seen, with 40 percent of individuals with SCD experiencing no episodes in a given year, and one to three percent experiencing six or more hospitalizations.

Biomarkers that predict children at greatest risk include low fetal hemoglobin (HbF), higher hematocrit or white cell count and a lack of hemolysis. Genetic markers of pain risk are currently being sought, and it is likely that such markers will be available as part of newborn screening in the next five years. These markers will allow us to individualize intervention therapy for children at high risk of frequent painful crises.

Care for SCD pain episodes begins at home, with the importance of active intervention being demonstrated in several studies. The La Rabida sickle cell disease program team spends a significant amount of time explaining the precipitating causes of pain and its care to the parent and child, with a focus on explaining the reasoning behind home interventions. Measures include adequate hydration at all times, the value of heat in increasing blood flow, and the use of non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen. Non-pharmacological interventions will also influence the psychological distress associated with an acute painful crisis. Approaches range from faith-based interventions to formal pain coping mechanisms taught by clinical psychologists. These strategies must be individualized to the child and family, and be regarded as a continuum with clinically based management.

Education is also provided on when to contact a physician, or the principles for a needs assessment in our Sickle Cell Program (or a local emergency room). Criteria include persistent pain that fails to resolve with NSAIDs, or pain associated with abdominal or neurologic symptoms, fever, acute chest syndrome, dactylitis, or priapism. Quantitative pain measurement is important, albeit subjective. We use the Wong-Baker FACES scale, with pain greater than four being a concern for clinical evaluation. Finally, it is critical that the child be assessed and receive effective therapy for asthma, or a co-morbid condition that can be associated with precipitating a painful crisis.

Patients with pain who present to the emergency room for possible hospitalization should be assessed in a focused, vigilant manner. New patients and/or their parents should be asked about what opioid preparation, route and frequency that facilitates ablation of a crisis. Opioids should be administered rapidly after presentation. Also, additional morbidity such as acute chest syndrome or stroke should be excluded using evidence-based approaches. NSAIDs, fluid resuscitation and antibiotics should also be considered.
The patient should be re-assessed using a quantitative pain scale frequently, and on a defined schedule. This review should occur at least every 30 minutes until pain has been terminated. It is likely that those children who do not respond to two to three appropriate doses of analgesia, spaced 30 minutes apart, will require admission. Breakthrough pain should be treated rapidly with an increase in either dose or frequency of opioids, and patient controlled analgesia (PCA) should be considered at an early time point.

The mean period of hospitalization for an acute crisis is 4.4 days. During this period, pain is controlled and education provided on potential options to reduce or ameliorate acute crises. It is also important to assess organ damage associated with pain - especially bony, neurologic, lung and abdominal SCD-associated injury. After discharge, the patient should be contacted in the first three days by the SCD team. This approach reduces hospital readmission of patients, and is a quality measure that is associated with a clinic review within one week of discharge by the SCD team in collaboration with the primary pediatrician.

How can painful crises be reduced in severity and/or eliminated? Enhanced fetal hemoglobin (HbF) levels in children with SCD have been shown to correlate with amelioration of the disease phenotype. Indeed, the fetal globin inducing agent hydroxyurea (HU), administered orally on a once daily basis, has altered the natural history of the acute painful crisis. There is general consensus among pediatric hematologists that patients with greater than two crises per year, frequent emergency department assessments for pain, or one episode of acute chest syndrome should be considered for long-term therapy. Less clear are the recommendations for priapism, renal disease or osteonecrosis, but patients are often initiated on therapy depending on disease phenotype specifics. In contrast, HU cannot replace transfusion as a mechanism of preventing stroke recurrence.

With HU, the number of painful crises and hospitalizations are reduced significantly. Initial management during the first year of therapy should occur in a sickle cell disease center, but subsequent monitoring can be performed by a primary pediatrician.

The patient must be informed that HU will not be effective in reducing the crisis risk without greater than 95 percent compliance with the daily regimen, that it will take three months to be effective, and that it may not have a significant impact on the risk of stroke. However, there is emerging evidence of its role in enhancing growth and development, improving splenic function, and preventing pulmonary hypertension and silent infarcts. Moreover, a major community concern has been the possibility that HU can induce a malignancy. However, it is clear from thousands of patient years of exposure to HU, that there is no increased risk, or indeed any other significant toxicity.

HU is a valuable addition to the therapy of severe SCD. Linking this chronic treatment with effective therapy algorithms for an acute crisis has allowed us to develop a pathway to care for children who present with this critical syndrome. New agents to reduce the incidence of painful crises either by increasing HbF or altering blood rheology are currently under evaluation. A remaining challenge is the chronic use of opioids in adolescents. However, we expect that the introduction of new predictors of prognosis and novel molecular-targeted agents is likely to improve SCD care. It is also likely that advances in stem cell transplant (see sidebar) may become more feasible for children with severe and recurrent painful crises.

It is an exciting time to be caring for children with severe SCD as treatment options expand. However, it will remain critical that we maintain the trust of our families and focus on exemplary patient care, introducing novel and potentially effective therapies in a thoughtful and collaborative manner with the SCD community.

Physicians, parents, and children with questions on the management of pain should contact Yasmin Abdullah at (773)256-5759.

(HU)

Sickle Cell Disease Screening

Radhika Peddinti, M.D., Yasmin Abdullah, A.P.N., and John M. Cunningham, M.D.

Newborn screening (NBS) for sickle cell disease was introduced in New York in 1975, in Illinois in 1989, and across the nation in 2005. It has altered the natural history of this disorder in childhood. The impetus for broad screening for sickle cell disease (SCD) was the observation that early diagnosis and initiation of penicillin prophylaxis was associated with a significant reduction in childhood morbidity and mortality. Subsequently, screening has also facilitated several other critical interventions including universal pneumococcal vaccination, the education of parents on detection of splenic sequestration, and the initiation of Transcranial Doppler screening for cerebrovascular disease.

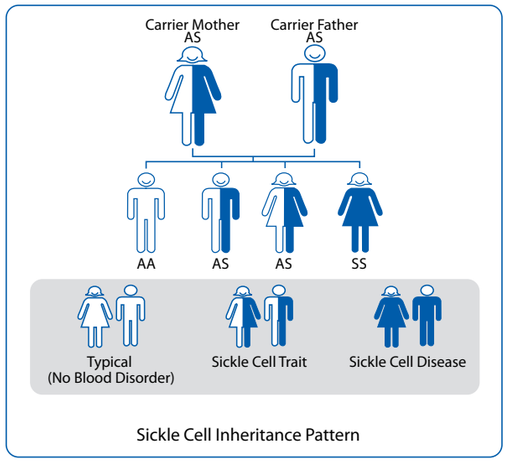
Three additional benefits are provided, but are difficult to quantify effectively, with early referral to a comprehensive, multidisciplinary SCD program. Firstly, the introduction of parents with a new baby with SCD to the clinical team provides an opportunity to receive education on the key issues that will face her child including early detection and prophylaxis for acute pain or infection, and screening for cerebrovascular, cardiopulmonary, and renal disease. Second, it allows for a discussion of the options available for ameliorative and curative therapies where appropriate. Finally, it represents a significant opportunity to meet and bond with other parents facing the challenge of raising a child with SCD.

What is the role of the primary pediatrician in NBS? Key roles include referral to and ongoing communication with a comprehensive SCD center like the La Rabida/University of Chicago Medicine program. This process includes arrangement of confirmatory disease testing, overall assessment, and development of a joint management plan for the individual child. This initial evaluation should occur within 8-12 weeks of birth to ensure the initiation of pneumococcal prophylaxis. The La Rabida/University of Chicago Medicine program team works closely with pediatricians to ensure that this process is effective, with a nurse practitioner and SCD physician working closely with the Illinois Department of Public Health and the community to ensure that no child is missed in this process.

Of equal importance is the counseling of parents and other family members regarding the disease and the carrier state. Recent studies of Illinois pediatricians suggest that although understanding of the disease among primary practitioners was high, several issues can still be challenging when advising family members. The education provided by our program, and by practitioners, must be complementary, explaining prevalence, diagnosis, disease pathophysiology, prophylaxis and treatment options, and the meaning of the sickle cell trait state. In the next paragraph, we provide a brief synopsis of the essential information provided currently to parents.

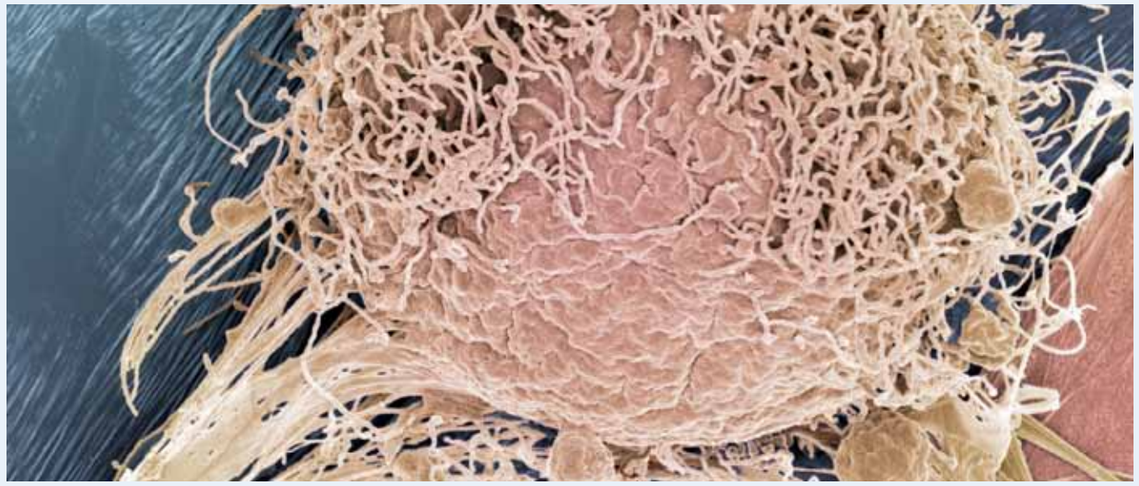
"A careful history and physical can help decide whether to treat this yourself or refer"

Approximately eight percent of African-Americans have the sickle cell trait. One of two parental copies of the beta-globin gene contains the sickle cell mutation (termed HbS). The autosomal recessive nature of the disease dictates a one in four chance that a child with SCD will be born to two parents who both have sickle cell trait. Approximately 80,000 Americans suffer from SCD. Given community misconceptions, it should be emphasized that to have SCD, each parent must carry at least one defective gene. In addition, it is important to explain that approximately 20 percent of children with SCD will have received one HbS gene, with the other defective gene being usually for beta-thalassemia (Hbβthal) or hemoglobin C (HbC). These distinctions are important as they alter the clinical severity, prog-



Sickle Cell Inheritance Pattern

(continued on page 8)


Bone marrow stem cell Credit: Paul Gunning / Photo Researchers, Inc

Stem Cell Transplantation: A Cure for Sickle Cell Disease

Patricia Engebretson, A.P.N., and John M. Cunningham, M.D.

This year marks the thirtieth anniversary of the cure of a child with sickle cell disease (SCD) using a matched sibling stem cell (bone marrow) transplant. This landmark report describes a child presenting with acute myeloid leukemia and SCD, who required a bone marrow transplant for her malignant disease. The cure of both diseases was a proof of principle that SCD could be corrected. This young woman has lived for many years with no evidence of either disease.

Her positive outcome was heralded by hematopoietic stem cell transplant (HSCT) physicians and by the general community. However, significant concerns were also expressed by the SCD community, and by physicians caring for these children, including potential acute and long-term transplant-related toxicities and procedure-related mortality. Furthermore, the therapeutic indications, long-term results, and the implications for children without a matched sibling remained unclear.

In this short review, we will address these issues, and future strategies that will allow an effective curative approach for all children with severe SCD who require a transplant.

Transplantation of more than 500 children with predominantly severe SCD has been reported. A consensus has developed regarding appropriate indications for matched sibling HSCT among SCD physicians, transplant programs, and the community. The criteria include stroke or silent infarct requiring hypertransfusion, recurrent acute chest syndrome (greater than two episodes/year), or frequent hospitalization for vaso-occlusive crises (greater than five episodes/year). These indications are based on the significant risk of morbidity and mortality (greater than ten percent) in severe SCD.

In contrast, children with abnormal cerebrovascular blood flow patterns, patients with frequent recurrent pain not requiring hospitalization, priapism, or dactylitis are not considered at this time. Lack of an appropriate sibling donor for almost 95 percent of children prevents many from availing the HSCT option. Currently, these children are offered enrollment on clinical trials of alternate donor SCT at University of Chicago Medicine, and other centers that specialize in this approach.

What should be the child's - and parents - expectations? In most HSCTs, a myeloablative approach using three chemotherapeutic agents (busulfan, Cytoxan, and antithymocyte globulin) administered over a seven day period results in complete destruction of the child's sickle bone marrow. Subsequently he/she received an intravenous infusion of bone marrow cells, the graft, harvested from the hips of the matched donor. Over the next 21-28 days, the patient and his/her parents remain in a specially designed hospital room that reduces the possibility of infection. When the graft starts working, the patient

(continued on page 8)

(Sickle Cell Screening continued from page 8)

nosis, and options for ameliorative therapy. Finally, we discuss the course of the disease, the need for physician assessment of all febrile illnesses, and the prophylactic and therapy options for infection, pain, and other complications.

Of course the majority of NBS results will show a child with the sickle cell trait. Although the need for education regarding SCD in this child is not warranted, this notification provides an opportunity to discuss the implications of the carrier state. From a clinical perspective, many physicians may not focus on these issues, given the supposedly benign nature of the sickle cell trait state. However, it is important to counsel that these children and their parent(s) may have increased incidences of hematuria, heat- and dehydration-induced rhabdomyolysis, hyposthenuria, splenic infarcts, renal medullary carcinoma, venous thromboembolism, or glaucoma after eye injuries. Of course, one in two children of any carrier will also be a carrier. However, care also must be taken not to overstate the concerns with sickle cell trait. For example, the recent decision by major college athletics programs to require screening of athletes for the sickle cell trait has been opposed by all professional societies and the Sickle Cell Disease Association of America as lacking clinical credibility.

In summary, the newborn screening for SCD has been a public health victory in changing the course of this devastating disease. We expect that with the imminent availability from advances in the Human Genome Project of genetic markers that identify children at risk from stroke, acute chest syndrome, and other life-threatening complications of SCD, that we will be able to tailor therapies that are specific to the individual child.

Physicians, parents, and children with questions on newborn screening for sickle cell disease should contact Yasmin Abdullah at (773)256-5759

(Stem Cell Transplantation continued from page 8)

is discharged and followed two to three times/week until 100 days post-transplant, then weekly until one year, and then monthly until two years post-transplant.

The results of large single center and multicenter studies have been outstanding. We have observed more than 93 percent of patients surviving this procedure. These results are tempered by transplant-related complications including viral illness, graft failure, and graft versus host disease (GvHD). Occurring in the first 100 days in up to 15 percent of recipients, these critical problems need close monitoring, and aggressive intervention; thus the frequent clinic visits.

Long-term, transplant-related complications center around the symptoms of chronic GvHD, which is severe in five percent of patients. Additional complications include sterility (< 40 percent), and pulmonary toxicity. These complications must be balanced by the significant advantages to the procedure including no vaso-occlusive crises, no stroke, no significant progression of chronic organ damage, and the restoration of normal growth and development. Together, these results confirm the efficacy and safety of the procedure in this high-risk population.

Interestingly, matched sibling HSCT has been used in SCD adults, but without success. In contrast, recent studies of a non-myeloablative or reduced intensity strategy in adults proved highly effective. We are now offering a similar approach in children, with the goal of reducing peri-transplant toxicity. Importantly, this SCT type has the added advantage of not being complicated with the long-term sequelae observed in the larger pediatric transplant population.

Finally, the work of many, including ourselves, is focused on the majority of children who have the SCD severity criteria necessary for transplant consideration, but lack a matched sibling donor. Approaches include the use of an unrelated cord blood graft or a mismatched parental transplant. Although our results, and those of others, are encouraging – albeit preliminary – we still face significant challenges. However, we anticipate that this approach will become fully available in the next five years for all patients with high-risk SCD. Alternatively, studies of other donor sources or a gene therapy replacement strategy show great promise.

We have made significant progress in developing a safe and effective cellular corrective therapy for some children with SCD who require curative intent. Our objective moving forward is to ensure that all children have unfettered access to a safe and efficacious HSCT.

Physicians, parents, and children interested in stem cell transplant therapy should contact Patty Engebretson at 773-834-0967

FALL 2012

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Thanks in advance for your help.

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
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The **MD to MD overview** in *MD Insights* is helpful.					
I enjoy the **information/education** articles.					
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Learning more about the expertise available at La Rabida, I am **more likely to refer patients** there.					
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STRIVE: A Health Mentoring Program for Teens with Sickle Cell

Marilyn Williams

This will be my third year with STRIVE Health Mentoring, Chicago; a program run by Next Step, The University of Chicago, and La Rabida Children's Hospital. Next Step facilitates programs that provide personal support, resources, and education to teens and young adults living with serious illnesses such as sickle cell disease. The STRIVE program is dedicated to helping teens living with sickle cell disease live full, healthy lives. This mission is accomplished through weekly sessions where lessons such as the biology and genetics of SCD, as well as the psychosocial issues that can arise from having a medically complex condition. We also provide one-on-one tutoring, an important component to the program since teens with SCD can miss several days or weeks of school due to pain crises, hospitalizations and other complications.

During my time with STRIVE, I have seen extremely shy kids come out of their shells, struggling and anxious students begin to talk about college plans, and patients understand the importance of listening to their doctors and becoming involved in managing their own health care. Ultimately, it is the "mentees" who both design the program and make it worthwhile for the mentors. Children with SCD have more responsibility placed on their shoulders at a younger age and have more serious consequences for shirking that responsibility than most of their peers. STRIVE acts as a supplement to familial support and medical treatment, helping with academics, teaching mentees to advocate for themselves, and connecting patients and families with others living with the same condition.

It has been my pleasure and privilege to work with this special program these past few years. STRIVE has been one of the most rewarding experiences of my undergraduate career and it is my greatest hope that the program continues to expand, acquiring more families and helping more teens with SCD.

Marilyn Williams is a fourth year undergraduate at the University of Chicago majoring in Classics.

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