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# Changing the Shape of Sickle Cell Disease Treatment: A Hermeneutic Study of a Case that Changed a Family and a Medical Practice

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## Abstract

This hermeneutic study analyzes a case of one family who chose to undergo two hematopoietic stem cell transplants for two of their four children affected with sickle cell disease (SCD) with full knowledge of the risks involved with curative therapy. This case had a life-changing impact on the family and on the medical practice of the physician who worked with them. As a result of this family, international treatment of early transplant for SCD has adopted different protocols. In this study, interviewing the mother in the family, the physician, and the transplant nurse, and analyzing the data hermeneutically brings us to a deeper understanding of how change occurs and its profound effect on lives and medical treatment.

## Keywords

Hermeneutics, sickle cell disease, change, family-health care professional relationships

Sickle cell disease (SCD) is the first human genetic condition that has ever been described, but it has only been curable since the 1980s (Johnson et al., 1984). Progress in the treatment of SCD has not come without a cost, and the decisions and choices that face families and physicians are complex and changing. In this hermeneutic study, we analyze the case of one family who chose to undergo two hematopoietic stem cell transplants for two of their four children knowing the risks involved with curative therapy. This case, as a result, had a profound impact on the family and also on the medical practice of the physician who worked with them.

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## Aim of the Study

Our aim in this study was to employ an in-depth analysis of one particular family-physician encounter with SCD and the decision to, knowing clearly the medical risks, proceed with the treatment approach of transplant rather than opting for the life-long risks of living with SCD. Through this endeavor, we gain insight into, and understanding of, the complexity of such decisions and the implications for future medical practice in this area.

## Background

Sickle cell disease is a genetic lifelong blood disorder, named as such because the red blood cells resemble the shape of a sickle (Quinn, 2013). Due to the errant shape of the red blood cell, these cells tend to lodge in joints and organs, resulting in pain and inflammation. It is also the first human genetic condition described at the molecular level (Serjeant, 2010). Until recently, the only course of treatment was medical management through means of symptomatic control through transfusions, medications, and hospitalizations for severe pain (Quinn, 2013). Worldwide, the life expectancy for someone with SCD varies based on cultural history and access to care. In the United States, for example, a life expectancy for men is 42 years and for women is 48 years (Platt et al., 1994; Quinn, 2004). In other countries, the life expectancy is not as high and the World Health Organization reports mortality rates in low-income countries as high as 50% by the age of 5 years (Lee, Thomas, Cupidore, Serjeant, & Serjeant, 1995; Odame, 2014). For perspective, the Jamaican SCD cohort study in the 1970s showed a 20% chance of being alive by age 20, and that standard of care remains the reality in some countries today (Odame, 2014).

Sickle cell disease was first noted to be curable in the 1980s when a child with both Acute Myeloid Leukemia (AML) and SCD had a hematopoietic cell transplant (HCT) and was cured of both (Johnson et al., 1984). Later that decade, a cohort of 12 children who were planning to return to Africa from Belgium all underwent matched sibling donor HCT and were cured (Vermylen et al., 1991). These children were returning to a setting of inherently greater medical risk due to endemic malarial infections and access to health care. This cure, however, was not without risks including graft versus host disease (GVHD), which can be life threatening and life limiting, infertility, or life threatening transplant related infections (Quinn, 2013).

In the 1990s, a landmark trial was published in the New England Journal of Medicine, which used the criteria that most HCT medical specialists have since adhered to in determining HCT eligibility for SCD (Walters et al., 1996). Under this regimen, cure rates were respectable; GVHD was relatively low, but some children died due to a disease-specific learning curve around supportive care. Sickle cell disease, therefore, is curable with HCT but still carries transplant associated risks, which must be weighed against the long-term risks of the disease (Bolañas-Meade & Brodsky, 2014; Quinn, 2013). The latter have been poorly defined, given how long we have known about SCD, and are in constant evolution given improvements in supportive care. A sickle cell crisis is a complication of these abnormally shaped cells blocking blood supply to bones (causing pain), brain (causing stroke or subclinical infarcts), kidneys (causing renal failure), lungs (causing respiratory and right-sided heart failure), spleen (causing infection or massive enlargement), and eyes (causing blindness). A crisis can be life threatening

and result in prolonged hospitalization for several weeks. Chronic breakdown of sickle cells leads to low hemoglobin or anemia, and intermittent or regular blood transfusions may be required to decrease symptoms. Stroke and subclinical cerebral infarctions affect over 10% of those who reach age 18 years (now 97% survive in North America to that age) (Quinn, 2013). In young adulthood, many individuals cannot work due to the inadequately described impact of SCD on the brain even in the absence of stroke (i.e., neurocognitive function) in addition to pulmonary hypertension, right sided heart failure, and renal disease. There is stigma associated with this disease, which results in denial on the part of patients and families, inadequate provision of emergency care for pain by health care professionals (even in Canada), and conditions where employers are unwilling to accommodate the sudden need to take time off of work for 1-2 weeks with a sickle cell crisis - - a crisis which could even be a life-threatening acute chest syndrome (Bediako, 2010; Butleer & Beltran, 1993; Freirermuth et al., 2014; Hank, Sackett, & Hartman, 2014).

Currently, with myeloablative HSCT, event free survival rates are as high as 95% with overall survival rates of 97% (events may include death or graft failure) (Bernaudin et al., 2007). Infertility is an expected side effect from HCT, and this – not the risk of death or GVHD - is often the reason many families say no to the transplant option. Dr. Greg Guilcher (co-investigator), along with others, has led the way in pediatrics in adopting reduced-intensity HCT, which can preserve fertility and is associated with 100% survival in those who engraft with no GVHD (the National Institutes of Health had one death in someone who did not engraft, and that person died of SCD, not HCT complications) (Hsieh et al., 2014).

As a result, if we can cure people with minimal risk and, in the worst-case scenario, they have SCD if they do not engraft, we feel this curative option should not wait for complications, such as stroke, that arise from SCD. The international literature and ethics conversations are also lining up with this view (Bolaños-Meade & Brodsky, 2014; Hsieh et al., 2014; Nicket, Hendrickson, & Haight, 2014; Roth, Krystal, Manwani, Driscoll, & Ricafort, 2012). Unrelated donor HSCT is still experimental; only 19% have an unaffected sibling match (i.e., 10/10 human leukocyte antigen [HLA] match and NOT affected by SCD) (Lee et al., 1995). Even for those who want to enrol in a clinical trial for unrelated HSCT, due to HLA diversity in people of African background (applicable to most but not all persons with SCD) and less representation on the donor registry, many cannot find matches (Guilcher, Fernandez, & Joffe, 2015). The genetic diversity in HLA phenotypes in individuals of African descent presents challenges for HCT.

These facts support the case that we present here as a basis for our study, a case that arose in Alberta Children's Hospital (ACH) and which, as a result of the treatment, changed not only the family but also the physician involved. The impact of this relationship has subsequently influenced treatment options for other families experiencing SCD.

In Dr. Guilcher's practice at ACH, one particular family was the first to request (or really politely demand) HCT for SCD for one of their children. In this family, there are four children: two born with SCD (Zaki and Abayomi; for confidentiality, the names have been changed) two without (Nkeoma and Ileara), with both of the unaffected children having each donated to a sibling. The father, when quoted all the risks of HCT, astutely stated that, in his view, they were comparable and not only acceptable, but preferable to the risks associated with a life of SCD. He

also described guilt in transmitting a genetic condition (although the inheritance requires genes from each parent) and the need to "undo what he had done." The family chose to undergo a full intensity myeloablative HCT for their son, Zaki, his twin sister, Ileara, being the donor. As a result, he is now cured with no major complications except (almost certainly) infertility. The family, while very happy with the outcome, requested to meet with Dr. Guilcher again after several years to discuss HCT for their youngest child, Abayomi, with SCD. Abayomi also received an HCT, although it was with a different, reduced-intensity regimen, thought to be fertility sparing. Abayomi is now cured of SCD; the oldest daughter, Nkeoma, was the donor.

The encounter with this family changed Dr. Guilcher's career as he examined the ethical issues of offering HCT to a child who had few complications of SCD (at the time of Zaki's transplant, HCT was only offered if specific criteria- now revised- were met). He struggled with taking the risk of HSCT without the child meeting criteria for eligibility that were accepted at the time. During the time when Dr. Guilcher and the family worked through the decision process together, the child had another pain crisis and the decision was made easier for all. Since this experience, Dr. Guilcher has been instrumental in building a national and increasingly internationally recognized program for the treatment of SCD using a reduced intensity HCT protocol, and this area has become his career passion. The family has demonstrated a willingness to be very open about their circumstances and experiences, volunteering their "case" to be used as an exemplar of how one family can make a difference, and in their case, change the face of the management and treatment of SCD.

## Research Design

### Method

This study was conducted through the research method of hermeneutic phenomenology. Hermeneutic inquiry is described as the practice and theory of interpretation and understanding in human contexts (Moules, 2002). It is a reflective, dialogic inquiry, concerned with understanding the world and the various forms in which understanding is manifested (Gadamer, 1960/1989; Moules, 2002; Moules, McCaffrey, Field, & Laing, 2015). Hermeneutics allows us, with the help of others, to make sense of the particulars of these contexts and arrive at deeper understandings. Hermeneutics nudges at the boundaries of the ways we think and converse about experiences and allows for language to give voice to experience that is often difficult to articulate. Hermeneutic phenomenology is a sophisticated method of research well documented and executed within the human sciences, particularly in health care research. Although philosophical in origin, hermeneutic research has been shown to have invaluable applied utility, offering insight into phenomena that has direct implications for practice (McCaffrey & Moules, 2016; Moules, Jardine, McCaffrey, & Brown, 2013; Moules, Jardine, McCaffrey, & Morck, 2011; Moules et al., 2015).

This is not a case study, which has its own methodology, but a hermeneutic study of a particular case. We do not mean to diminish the family by classifying them as a case; we think rather of case in relation to its original meaning:

> The word "case," long since incorporated into medical, legal, and other professional speech, has this sense of arrival in its origin. Case derives from the Latin *casus*, meaning a chance, occasion, opportunity, accident, mishap. Literally, it means "a falling." In the 13th century, it had the meaning of "what befalls one" and in the 18th century began to be adopted by medicine. (Moules et al., 2013, p. 3)

This family then befell Dr. Guilcher and the case itself became an occasion and opportunity that was life changing. Hermeneutics is a method that honors the particular and an in-depth hermeneutic study can be conducted with as much thoroughness and rigor with an n=1 as with an n=10 (Moules et al., 2013; Moules et al., 2015). It has been convincingly argued that sound qualitative research provides different answers to questions, and therefore different kinds of understanding than does research that uses measurement tools (Moules et al., 2015). It offers the opportunity to conduct a more thoughtful, effective, skillful, and humane practice in contexts where prescriptive and assumed practices do not adequately satisfy the complexity of the situation.

## Data Collection

After ethical approval was granted by the University of Calgary Conjoint Health Research Ethics Board, the Principal Investigator (Moules) conducted in-depth interviews with the mother of the family, the allogeneic HCT primary nurse/transplant nurse coordinator who was involved with both children, and with the HCT physician. The physician is also a co-investigator in this study, but hermeneutics, as a method, allows for researchers to also be participants; in fact, it argues that they always are to some extent. The interviews were audiotaped and transcribed verbatim for purposes of hermeneutic analysis. The transcribed interviews were then reviewed by the physician who wrote an additional reflection based on them. All of this work culminated in approximately 70 pages of single spaced data in textual form.

## Data Analysis

In hermeneutics, analysis is synonymous with interpretation, which occurs in the complex dialectic of research interviews with participants and interpretive memos written by the researchers based on the transcripts. Qualitative software is not used in analysis because hermeneutic interpretation is not based on thematic analysis or a search for recurring themes. Software data analysis is unable to attend to the particular. We begin interpretations through a careful reading and re-reading of the data, looking for statements and instances that resonate with the researcher and provide an opening for understanding. In other words, we look for statements in the data that have "grab" in that they catch our attention and appear as avenues to shed light on the phenomenon under investigation. The initial individual interpretations of researchers are then raised to another level of interpretive analysis in the research team's conversations through in-depth, rigorous, reflexive, and communal attention to the data. Hermeneutic work not only generates a rich description of the phenomenon, but it must also strengthen the description through exemplars and rich data. In the arrival at interpretations, particular criteria guide the analysis: agreement, coherence, comprehensiveness, potential, and penetration (Madison, 1988; Moules et al., 2015). Unlike some other qualitative methods, hermeneutics is not in search of themes, semantic coding, constructs, or theories, but rather seeks events of understanding to

deepen understanding of a topic in such a way that it can be seen differently and can ultimately be practiced differently (Moules et al., 2015).

## The Family

For purposes of confidentiality, only some aspects of the family will be described here. The family structure consists of a father and mother (both carriers of SCD) and four children, the eldest being at the time of the research 13 years, then twins at 10 years of age, and a younger daughter who was 5 years old at the time of the research interviews. The male child of the twins and the youngest child were affected with SCD, and the other two children were matches for transplant. Only the mother agreed to be interviewed for this study, and we admit that her perspectives might not be representative of the father's or of the children. The interviewer, however, by way of observer perspective questioning (Moules et al., 2015; Wright & Bell, 2009; Wright & Leahey, 1990, 1994, 2000, 2005, 2009, 2013; Wright, Watson, & Bell, 1996) attempted to elicit other members' perspectives. The mother represents the voice of the family for this study.

## The Nurse

The nurse in this study is the allogeneic HCT primary nurse and transplant nurse coordinator at Alberta Children's Hospital for the Bone Marrow Transplant Program for Alberta. At the time of the interview, she had been in this position for 10 years, but had worked in hematology/oncology for over 25 years. She worked with the family in the cases of both transplants of their children.

## The Physician

The physician in this study (and co-investigator) is a pediatric oncologist and bone marrow transplant physician at Alberta Children's Hospital and an Assistant Professor of Oncology and Pediatrics at the University of Calgary. At the time, when this family came to his care, he considered himself *"fairly junior…only in practice a couple of years."*

## The "Case"

The following is a description of the co-investigator/physician's (Guilcher) experience with this family, written by him after reviewing the interview transcriptions.

*Our sickle cell transplant program started in 2009, when this particular family requested a consultation. Zaki was affected with SCD, and had had some complications from the disorder. Ileara was identified as a 10/10 HLA match, and did not have SCD. The family wanted a cure. They came to the meeting ready to organize a transplant.*

*Bone Marrow Transplant (BMT) for SCD has a 30-year history, only for those with matched siblings who do not have SCD. The first case was a child who also had AML, was transplanted and cured of both. The next group were children who were transplanted as they would most likely die of SCD upon their return to Africa from Europe. Then came clinical trials which*

*showed high rates of success. These trials, however, had specific inclusion criteria as do any clinical trials. These criteria are to ensure the ethical conduct of the research and subject safety.*

*In Zaki's case, he did not meet those criteria established for the prior research trials. But his family was not looking to participate in research - - they accepted the data from those trials and felt the benefits outweighed the risks. They felt that transplanting before Zaki developed many sickle cell complications was the right thing to do to avoid those complications - - complications such as stroke, lung and heart disease, kidney failure and more. His father could quote these risks of SCD, and wanted to take away this disease that he felt responsible for giving to his son.*

*We agreed that the family had a valid case for transplant. We also wished to spare him of those life-threatening and life-limiting complications of SCD. However, we wondered if the family really understood the risks of BMT: GVHD is an abstract concept until your child is living with it. But does any family truly understand these risks? Yet we accept their consent for BMT. We also debated whether the generally accepted criteria for BMT for SCD must be adhered to now that those trials were complete and the data available (the need for a child to have a severe enough phenotype, yet adequately preserved end organ function). Do these criteria still hold now that the data are available, or is it still justifiable to apply them prospectively to ensure BMT is not used too liberally with its inherent risks? The family did not need to debate these points, but we did. We owe families autonomy to choose for their children, but we must also seek to do no harm, or minimize this harm. In the end, we felt we could honour their request, but Zaki ultimately met the established criteria before BMT anyway, having developed another painful crisis in the meantime. In the process, we were challenged in a healthy and productive way. We consulted within ourselves and abroad, and grew in the process. We explored these important points of tension deeply, and felt we understood them better. We still struggled with the infertility risk associated with BMT for SCD using protocols established at the time.*

*Zaki did very well. He still is doing well. We were relieved and proud. The family was happy.*

*Then Abayomi was born with SCD. She was born the same week as my daughter, at the same hospital. She feels like a daughter to me. I was sad for the family, and offered to discuss BMT when they were ready. We typically don't offer BMT before 3 years of age for these "elective" indications.*

*Eventually, Oluchi (mother) was ready to talk about BMT. She requested a meeting, and was pleased to hear that we had adopted a newer protocol with fewer toxicities and one which does not usually compromise fertility. With Nkeoma identified as a match and keen to donate, Oluchi asked us to transplant Abayomi. At this point, with the very high rates of success, low risk of infertility, and no reported cases of GVHD with this new approach, we were ready to move ahead. I should note that another family respectfully challenged us to adopt the new protocol, which we did once sufficient data were available to document it was safe and successful in adults. There was no reason to believe it would be riskier to use it in children. We believe we have the only experience with its use in children in the world.*

*Abayomi did well. She had an easier course than Zaki, with a shorter time in hospital, as would be expected with a "lighter" protocol. This conditioning regimen involves immune suppression*

*and a low dose of total body irradiation- no cytotoxic chemotherapy. The family went from two children with SCD and an uncertain future and life-expectancy to four children without the blood disorder.*

*We all celebrated.*

*This family has changed my career, and my life as a result. They challenged my practice and way of thinking. They did so in a considerate way, out of a duty to advocate for their children. We worked through the tension of different viewpoints with respect, and all of us grew in the process. At least I can say our team did. I certainly did. They changed our practice - physicians, nurses, pharmacists, social workers - the list goes on. Our criteria for offering BMT for SCD changed as a result. Many children have undergone BMT since we met this family. All of these children are cured and well.*

*Our hospital has developed a program which provides excellent care for those who cannot undergo BMT for SCD due to lack of a family donor. We have a world class hemoglobinopathy clinic. But families want a cure. We want to cure them, but we want to do it safely. We do not want any child to die as a result of BMT, or develop major complications. However, some children will have life threatening complications from SCD, so we need to have more options for those children without family matches. So, we have opened clinical trials for children who only have unrelated donors. Again, we have safety criteria to be eligible for such trials to make sure we do things in the right way before we have data. The data that exist for unrelated donor BMT show these children get many complications. But we will keep trying to learn more and find better ways.*

*We have participated in the establishment of the Sickle Transplant Alliance for Research (STAR), an international consortium dedicated to finding more cures through BMT for SCD - - cures for more children with fewer complications. We have a vision of helping in the development of more comprehensive sickle cell disease programs in Africa. With 50% of children in the poorest countries dying before age 5, we have a lot of work left to do. I believe we can bring BMT to Africa and cure more children, not just those in countries with more resources. This work has already begun with friends and colleagues in Nairobi, Kenya, and Mbarara, Uganda. Alberta Children's Hospital and the University of Calgary have become leaders, and are advancing the field of SCD disease care and BMT.*

*This story started with Zaki and his parents advocating for him. Many parents have followed. I am humbled by their trust and respect. This family changed my practice, and my life as a result. The "Butterfly Effect" continues.*

*I am grateful to them.*

## An Interpretive Analysis of the Case

In hermeneutic interpretation, we weave the voices of the participants with the interpretive reach of the researchers. Interpretation is aimed at starting from, extending, and then returning to the participant's experiences and understandings in such a way that the topic under investigation can

be understood anew and deeply. Participant quotes are presented in italics and identified as mother, nurse, or physician.

**Being Heard: "I'm not going anywhere because there is something wrong with him"**

For this family, the first instance they faced around needing to convince healthcare professionals came during the first pain crisis experienced by their son at 14 months of age. After two visits to emergency and being sent home after being told that nothing was wrong, the mother refused to leave without further investigation. Fortunately, at her insistence, a doctor came on duty who had worked in Atlanta and was familiar with SCD and suggested the son be tested. The mother's knowledge that the fact that her son could no longer walk was warranted both in physical evidence and in a mother's intuition that something was wrong. A young child unable to weight bear could be dismissed but it warranted some investigation. The early tests in emergency, however, missed the later discovery that a blood clot in his hip had developed into an infection. Only after the SCD testing was initiated, did the full diagnosis of the clot and infection arise. This missed diagnosis resulted in a 3-month hospital stay and an introduction to the physician who would eventually change their lives.

"Being heard" arose again in this family's experience around their request for a transplant without meeting the criteria for transplant. In consideration of this request, the physician had to gather his own experience and his faith in research that was almost 20 years old.

> *There were historic criteria for transplant that were based on a publication that is now almost 20 years old, which made sense to have inclusion and exclusion criteria. Of course, being a researcher myself, I believe in those criteria but they've been perpetuated as the criteria for which a transplant for SCD should or should not be performed. (Physician)*

Against scientific "evidence" and guidelines, this physician was faced with the dilemma of who to hear and to whom to listen.

> *When the family first approached us, they were adamant they wanted the procedure done and the child had not met the criteria…so not having a lot of experience for transplant for SCD and a child who did not meet what might have been rightly or wrongly accepted criteria for transplant, we were hesitant to subject him to a potentially life threatening procedure without that experience and without those criteria having been met. That was an issue for us more than the family. (Physician)*

Literature on the knowledge of parents about the condition of their child or that "something is wrong" despite medical professionals indicating the opposite has been documented in health care literature (see Farde & Linja, for e.g.). The intersection of the expertise of healthcare professionals and the expertise of families (Wright & Bell, 2009; Wright et al., 1996) is shown here in both in the mother's experience of finally being heard in the emergency department that something was wrong and, later, in the family's approach to the physician.

**Weighing the Risks**

As time continued and more pain crises occurred, the family was clearly informed about the option of transplant.

> *They gave us options to see if there was a chance for a transplant, how life would look like. And then we figured out both ways if he didn't have the transplant or if he had it, how it affected his life…if he would just live the deficient life, a transplant for him was better at the time…worth the risks. (Mother)*

The risks presented to the family were out of concern and experience.

> *The family said we acknowledge that these criteria have existed in the past, but were able to quote the risks of a lifetime of SCD and said that nothing they had heard about a transplant was worse than what they were anticipating for their child with SCD. Which, with the eye of retrospect, I certainly agree - and I've been converted if you will - but this is also from a family who had not seen a child die of GVHD or transplant related complications. So, it's one thing to say they understood those risks, which… this will sound contradictory given that we get "informed consent" for transplant all the time but I don't really believe a family really gets it until they live it and they all live it differently so a family who has not had GVHD or a life-threatening complication of transplant will look at transplant differently than a family who has. (Physician)*

The risks, as the mother understood it, were GVHD and infertility but, in their minds, the risks of him living with this disease were even worse than these possibilities. Seeing her child in recurring pain was tormenting for them as parents.

> *In the middle of the night he would just be in pain and there was nothing you can do to help him, you know. (Mother)*

As a parent, seeing your child in pain is unbearable. Often overlooked clinically, the parental response to seeing their child in pain can have effects on both the parent and the child at cognitive, behavioral, and neurobiological levels (Simons, Goubert, Vervoort, & Borsook, 2016). The needs of a parent whose child is suffering with chronic pain, while currently not well understood, is an emerging focus of research (Palermo, Valrie, & Karlson, 2014; Vervoort, Trost, Sutterlin, Caes, & Moors, 2014), as it is recognized that the resultant, sometimes maladaptive, behavioral responses of parents may influence the treatment outcomes of their child (Simons et al., 2016). The complexity of parent-child interactions in the context of childhood pain in an important consideration within the treatment of SCD, given both the acute and chronic nature of pain experienced by these children.

> *You're just watching him while he's sleeping throughout the night because you don't want him to stop breathing…you don't want to wake up in the morning and he is not awake…so I stay awake at night just to watch him breathe…yeah, it was really huge. (Mother)*

There was some division in the beginning in terms of the family's wishes and their claims to understand the risks and what was involved and what the medical team perceived to be as accepted practice, but the family remained committed to their decision.

> *They were committed to transplant…there was a meeting but my recollection was that in their minds, the meeting was not to decide but to talk about how to make it happen…their minds were made up before ours were. (Physician)*

However, despite the disparity, two other things happened to intervene on the decision:

> *One, we had a visiting professor who is one of the world leaders in SCD…who comes from Ghana, so he's got a cultural perspective as well...that supported us in that if we felt the family truly understood the risks and benefits, that it was reasonable to provide the therapy. And secondly, in the course of this discussion, he (child) had another one or two pain crises that made him fit the historic eligibility criteria. (Physician)*

At two and a half years of age, his twin sister was found to be a match for transplant and a successful transplant ensued. At the time of the interview, Zaki was 10 years old, a normal, healthy kid.

> *And you wouldn't even know. He plays basketball now, he plays sports, he's active and he can exercise and run. I never had any regrets because I felt it was better and the most important thing is his organs were really intact; none of the organs were destroyed, spleen kidney, everything was fine, so I mean it's still excellent so I think it's the right decision we made. If he still be Sickle Cell, he'll be on this one medication for life till he dies. (Mother)*

The nurse spoke of the sense of anticipation and interest that this transplant irrupted in the clinical area.

> *He was the first I believe, the first if not one of the first sickle cell transplants that we did here at Children's. And I remember at the time you know there was a certain amount of excitement and you know interest and so on because it was the first one. But I do remember also being a little bit unsure about the unknowns as well because it was the first one we had done and not really knowing what to expect with respect to how he would respond, how ill he would become, you know and then what would the outcome and follow-up piece look like you know how would he do. So, I remember that piece, I do remember the family when I first met them I also felt that there was a little bit of pressure from the family, especially, to get this done and, in a sense, wondering if they truly understood the implications you know of going forward on this particular protocol. Because it was such a high dose toxic regimen. And also the third piece that really resonated with me was the sense of like the family, because we were not familiar, a familiar team, I also felt there was this feeling of sort of that trust, right, you know in being able to hand over their trust to us. You know there was that bit of transition as well. (Nurse)*

> *From the family, you felt they were checking you out? (Interviewer)*
>
> *From the family, yeah. Because they're I think you know they had been followed for so long by the hemoglobinopathy team and you know you build the trust with the team that you're most familiar with and so we were a new team and sort of when you mentioned about the mom being a little shy at the beginning of her interview that is exactly what I recall when we first started working with her as well, she was a very sort of shy almost a little… not standoffish but just very guarded I would say. (Nurse)*

The confluence of the two events of the visiting professor and the new pain crises solved the ethical and medical dilemma faced by the medical team.

> *We could answer to ourselves or to anyone who had asked, well he had met these medical criteria, we had gone through what we thought was due diligence with the family and then we had consulted with someone from outside our program and this relationship with the family, who also supported our thinking that even if the child had not had these additional pain crises that the family was adequately informed and we weren't doing anything unethical. So, that led up to the first transplant for this family and for our program. (Physician)*

The family too demonstrated their astute knowledge of the risks of treating and the risks of not treating.

> *I thought a part of their motivation to fix this disorder was connected to their sense of guilt about having given it to their child, but when they told me a clear description of what a life of SCD would be, including them quoting statistics of risk of stroke, lung disease, and right sided heart failure…the father in his mind matched them all up and said "well there's still nothing you've said that is worse than what I know we face as a family with a child with SCD." (Physician)*

**Changing the Future: Convictions and Stereotypes**

> *So, then that was the first transplant successful…in terms of curing the child, he had no major unexpected complications, the family is happy with their experience to the point that they wanted to pursue transplant again for a second child, which I thinking was probably as much proof that they thought it was worthwhile out of any. (Physician)*

Like all situations, context is complex. One of the things that emerged in the interview with the physician was the issue of stereotyping. Between families in the communities where SCD most often occurs, news of the early transplant was circulated, and within the local ethnic community where SCD is most prominent, there was open discussion about it. Alberta, however, stands in contrast to many other American and Canadian SCD communities because it is mostly first generation Canadian, whereas other locations have multi-generational histories that may contain some embedded apprehension and distrust of the medical system. There is a history of racially, and often financially disadvantaged families that already feel marginalized and perhaps not in a position to engage with healthcare professionals with confidence.

> *…lack of connection with the medical community and some of it is certainly the fault of healthcare providers given that this is a disease that is commonly associated with severe pain and people who live with severe pain and when they present with a painful crisis which is by the description of those who have such crises extraordinary painful and certainly and the source of the pain is generally lack of good blood supply to the bone and when we see this in certain malignant conditions we have we know those kids are in extraordinary pain. These kids with Sickle Cell or these young people learn to live with it a bit better or a bit I shouldn't say a bit better; they are more familiar with the pain and they find a way to cope because they have to and perhaps their outward manifestation of such pain is less evident… Presents in a different way they also might not look as distressed as a healthcare provider might assume they should look for the amount of pain they are describing because the standard of care is aggressive narcotic treatment and that combined with being perhaps from a marginalized community leads to distrust from a lot of care providers and a delay in providing adequate medical care including pain relief. That is a common stereotype and then there's a reluctance for patients with SCD to pursue medical care when they might otherwise need it because they're fearful of that experience. They, like any person, [find] that judgement is very upsetting to them and after so many experiences of going to an emergency room to say "I'm in extreme pain" and have someone disbelieve them - then that's where medical care providers have played a part in creating a divide between these families and care providers so that and this situation in the US is the same or worse where there's an even longer more complicated racial history, I think most people would say, not that Canada has a perfect history by any stretch, but I think the history with slavery is longer than that with Canada and the African American population is larger and I think it's fair to say that political sociologic history is much more well known to people and entrenched. (Physician)*

This is a context in which stereotypes and political, sociologic, and racial histories play a role. These issues perhaps have had effects on treatment approaches. A part of changing the future of transplant and SCD treatment locally for Dr. Guilcher also included acknowledging this history that is well entrenched in parts of the world. The medical community, however, in the face of new evidence such as provided by this encounter with this family has also addressed old biases and beliefs and there has been a ripple effect of treatment changes in the world of SCD.

**Facing it Again: Relationships Already Formed**

When their youngest child was born, the family waited until she was six months old to test her for SCD. Though she had no symptoms, the results came back positive for SCD. She was not as ill as her brother had been, yet she did eventually have some pain crises requiring hospitalization and, at 3 years of age, had her transplant with her oldest sister as the donor.

> *I told Dr. Guilcher, you know what my decision will be, so he said okay, he will be here for her if she had Sickle Cell, and that's how it went. She was waitlisted, but he had a cancelation…so that is why she went. (Mother)*

The physician was curious initially why the family did not immediately approach him with the same enthusiasm for immediate transplant, and surmised it was multifactorial.

> *I think first of all she was very young. I wondered if it was in part due to the fertility and perhaps cultural views of gender and fertility…it's not that she waited to see how severe her SCD phenotype would be. Which is what most hematologists and transplant physicians would want to see before offering transplant, but that was not at the heart of her coming to us. I guess she was ready is how she expressed it. (Physician)*

Eventually, the family made the decision and the older sister willingly became the donor.

> *She wasn't afraid. Once she knew that she could help her sister, she was happy to do that and there wasn't like a second thought. (Mother)*

With advances in treatment, the younger sister received a less aggressive form of transplant that was intended to preserve her fertility.

> *Fortunately, our clinical practice had evolved as I mentioned offering RIC [reduced-intensity conditioning] and she was very excited to hear about a different option that offered the same high rates of success but less toxicity as well as more, a difference of an 85% infertility rate with myeloablative transplant compared to no expected adverse impact on the child's fertility. (Physician)*

The mother considered this advancement as

> *Huge for the system so that people will not be scared because like something might be scared oh why won't my kids have kids, right? (Mother)*

The second time around with this family was experienced as different for the nurse.

> *Completely different because obviously that trust was already there. I felt, with mom, the sense of the stress level in going through it again was certainly considerably lower because she had already had that prior experience of what to expect. And then, compounded with the fact that it was a much-reduced intensity so even less of a concern on her part, and knowing that son did so well even with the high intensity protocol, it was so much easier. It sort of set the tone for the relationship the second time around as she already had that feeling of security and trust. (Nurse)*

The tone of trust and familiarity that this nurse speaks of is integral to a relationship that works in healthcare settings (Robinson, 1996), a relational stance of collaboration and trust. This family was known by the team and the team was known by them. McLeod, Tapp, Moules, and Campbell (2010) wrote about the impact on knowing and being known in relationships between nurses and families. In fact, the little girl was introduced to the certain members of the team from the time of birth through the treatments of her brother.

> *So, we sort of were introduced to her right from Day One so to speak, so even going through her you know from infancy right through to the time that she was transplanted. (Nurse)*

This family had perhaps been through relational components that form in healthcare situations, moving through naïve trust to a place of a guarded alliance, where consumerism and team playing take shape (Thorne & Robinson, 1989).

## Discussion: Change and Making a Difference

> *I would recommend it to any family that has a sickle cell kid and if there is a match in the family, they should go ahead with it and because there is not any risk – not being able to have kids so the risk is very very low. They give opportunity to the kids to have a second life. They are not going to be sad, not going to be unhappy, and they're going to appreciate their life. I think that's huge. He (Dr. Guilcher) gave our family a second life – like he believed he could do it and then he did it and it was successful by the grace of God. (Mother)*

Practice changes and treatment changes, all change for that matter, are not always seamless and easy. Even good changes require adjustment. This case that changed the medical practice for one physician has had a global ripple effect on the treatment of SCD. Starting transplants earlier in the SCD trajectory broke a protocol that held precedence over judgement.

> *…a good thing from a toxicity perspective, a recovery perspective, and sort of long term related effects perspective definitely. Now mind you, with some of these reduced intensity protocols, we're still learning and still collecting data of course, but I feel like it's very hopeful and it's certainly opening up a whole new group of diagnoses who in the past were maybe not eligible to even consider transplant as a curative treatment…the sky's the limit really…if you consider the chronicity of the illness and the impact on healthcare and healthcare dollars… (Nurse)*

Change depends on difference; a difference has to be noticed to make a change. The terms "news of difference" and "difference which makes a difference" are associated with the onetime revolutionary anthropologist, Gregory Bateson. In his teachings of difference, Bateson (1979) offered a metaphor of the weather, suggesting that the weather is in a constant state of change of which we are aware on a day to day or even moment to moment basis, but he questioned if it is changing from year to year. He maintained that we cannot know this without detailed study, as it is a gradient of difference beneath our ability to discern. Since the mind can receive news only of difference, "there is a difficulty in discriminating between a slow change and a state. There is necessarily a threshold of gradient below which gradient cannot be perceived" (Bateson, 1979, p. 98). Bateson (1979) went on to suggest:

> Similarly, it is very difficult for us to perceive changes in our own social affairs, in the ecology around us…it is a nontrivial matter that we are almost always unaware of trends in our changes of state. There is a quasi-scientific fable that if you can get a frog to sit quietly in a saucepan of cold water, and if you then raise the temperature of the water

> very slowly and smoothly so that there is no moment marked to be the moment at which the frog would jump, he will never jump. He will get boiled. (p. 98)

> *This family were kind of the starting point…the beginning of this new sort of era…sort of cutting edge in a way…led us to where we are now. (Nurse)*

This family was the difference that made a difference and heralded change, not just in one physician's practice but internationally.

> *My practice changed because of this family really…So we offered sickle cell transplantation to this family so we then could no longer say to ourselves or to those who came to us that we hadn't done this before. We had learned, fortunately through the literature and not through bad experiences, there are very unique supportive care measures for SCD transplantation that are distinct from routine transplant supportive care which I don't think are really the focus of this study. We learned about that in the process and that was intellectually challenging and stimulating. But then came the ongoing and continuing relationship with our hematology colleagues for referrals and requests from families. Referrals which have led to a series of children who have been transplanted. Such that outside of Montréal, we've done the most of any centre in Canada. And I think that, not that it's about who does the most, but we could foreseeably become the most experienced centre in Canada with transplant. We have a series of research collaborations and local research projects that are advancing the field and catching people's attention… joined, because this is become a marriage of transplant and sickle cell care for me it's something I'm very passionate about. I heard Steve Jobs said once before he died that when you're passionate about something that work pulls you instead of having to push yourself to do it and that's what I really found here when I was looking for an area of interest within my practice and had dabbled in a few areas such as, which are still very interesting to me, bioethics and adolescent young adult oncology care. And I'm still interested in those areas but none so much as this, I just knew that this is what I loved and wanted to do and so when an opportunity, when I heard about a North American consortium was starting as a grass roots group of people who had started some conference calls because this is also what they loved and I could tell when I only happened upon this through speaking to one of my transplant colleagues about another project she was doing for a different hemoglobin disorder called thalassemia and she mentioned this. Then it wasn't, for me, it wasn't a question of if I could participate; I had to be a part of it. And then the person leading the charge is someone I had worked with in other Children's Oncology Group work and when I spoke to him I could tell he was initially reluctant because they were trying not to just grow their numbers of participants without some degree of caution but in my head and in my heart, I wasn't taking no for an answer and I have been a very, I think I have been a very valuable contributor within that group and the only Canadian contributor. So, we are the only Canadian centre part of this consortium which is developing registry work in clinical trials and advocacy work for sickle cell transplantation so and so these are really the leading Sickle Cell transplant physicians anyway in North America and I'm becoming increasingly respected within that group and within Canada. It has really launched my career and it really changed the life of this family. (Physician)*

## Summary: Changing Shapes

Through a rigorous hermeneutic analysis of one case of a family facing life with two children living with SCD, and choosing a treatment path that was, at the time, not the first recommendation of physicians, we examine how this family changed the medical practice of one physician. In turn, he has had an influence on other medical practitioners in his field, and the approach to treatment of SCD. More importantly, this family now has four healthy children.

The arrival of one family matters. Moules et al. (2013) wrote of the power of the individual case in the context of oncology and how the renowned medical oncologist, Dr. Robert Buckman, was reported to have commented that it was the individual case that changed his practice always. He claimed he could not walk into a new patient's room without his practice being forever changed.

> In this regard, Dr. Buckman was arguing for something subtly hermeneutic about his practice and about the knowledge that arises only in practice. It was not simply that the individual patient was more important than his aggregate knowledge…but that the confrontation with the individual, the particular, always enlivened, challenged, and informed that knowledge, keeping it awake, alert, and in proper perspective…The next case always seemed to arrive as an opportunity to open up his vast knowledge and to let it be susceptible to what enlivening difference this new arrival might make. (Moules et al., 2013, p. 3)

We believe this intensive analysis of this case, an n=1, which in traditional approaches to scientific understanding would be dismissed based on this very fact, has the potential to change the "shape" of treatment of SCD worldwide. In fact, we know it already has.

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