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Reflections

# Caring for Transplant Recipients in a Setting of Restricted Resources

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"*Courage is grace under pressure*"

Ernest Hemingway from a 1926 letter to F. Scott Fitzgerald

The above quote from Hemingway (figure 1) exemplifies the spirit of the people and transplant practitioners of Cuba. This island nation is home to approximately 10 million people, about the same population as Georgia or North Carolina. Yet the gross domestic product per capita of the two US states ($61,500-$74,000) far exceeds that of Cuba ($7,200). Since the fall of the former Soviet Union, Cuba's international trade has dwindled and the economy has further contracted requiring constant repair of aging machinery and automobiles (figure 2). With continuing economic embargos, there are rolling power outages and limited access to medicines and medical equipment. Hardships are compounded during hurricane season when storms damage hospitals (figure 3), interrupt supply chains and further increase medical supply shortages. In this setting of severely restricted resources, how do stem cell transplant centers even function?

## CALIXTO HERNANDEZ CRUZ

Hematopoietic stem cell transplantation (HSCT) began in Cuba in Havana in 1985 at the Institute of Hematology and Immunology (IHI) and the Hermanos Ameijeiras Hospital (HAH). This was followed by units at CIMEQ hospital (also in Havana), at the Arnaldo Milián Hospital in the center of the country (Villa Clara province) and the Lucía Íñiguez Hospital in the east (Holguín province). Centers in Havana perform both autologous and allogeneic transplants, but only the IHI performs pediatric transplants. The HAH in Havana is the largest tertiary center for adults and has beds dedicated exclusively for acute leukemia and HSCT. To date, 599 blood and bone marrow transplants (BMT) have been carried out in Cuba in the five centers, the majority being autologous stem cell grafts.

During the 1980s, the initial challenge was the introduction of HSCT into Cuba, a process skillfully led by our beloved professor Dr. José Carnot Uria at the HAH center. With the collapse of trade with the former Soviet Union and the intensification of the economic embargo on Cuba, long-standing economic deficiencies rapidly increased. The country and its health system managed to blunt this to some extent, so that transplant activity was maintained despite significant adversities. As the economic situation slowly improved, HSCT programs gradually expanded. With cooperation initiated by the University of Illinois at Chicago (UIC) starting in 2016 and the subsequent experience gained, HSCT momentum accelerated with 81 transplants performed at HAH between 2014 and 2018, 57 autologous (70%) and 24 allogeneic (30%). On average, 16 transplants have been performed each year. Half of the allogenic HSCTs were haploidentical transplants, as a result of the collaboration with UIC. A total of 6 individuals (3 allo and 3 auto) died within the first 100 days after transplantation, with an overall day 100 transplant-related mortality of 7% (*Rev Cubana Hematol Inmunol Hemoter,* December 2018).

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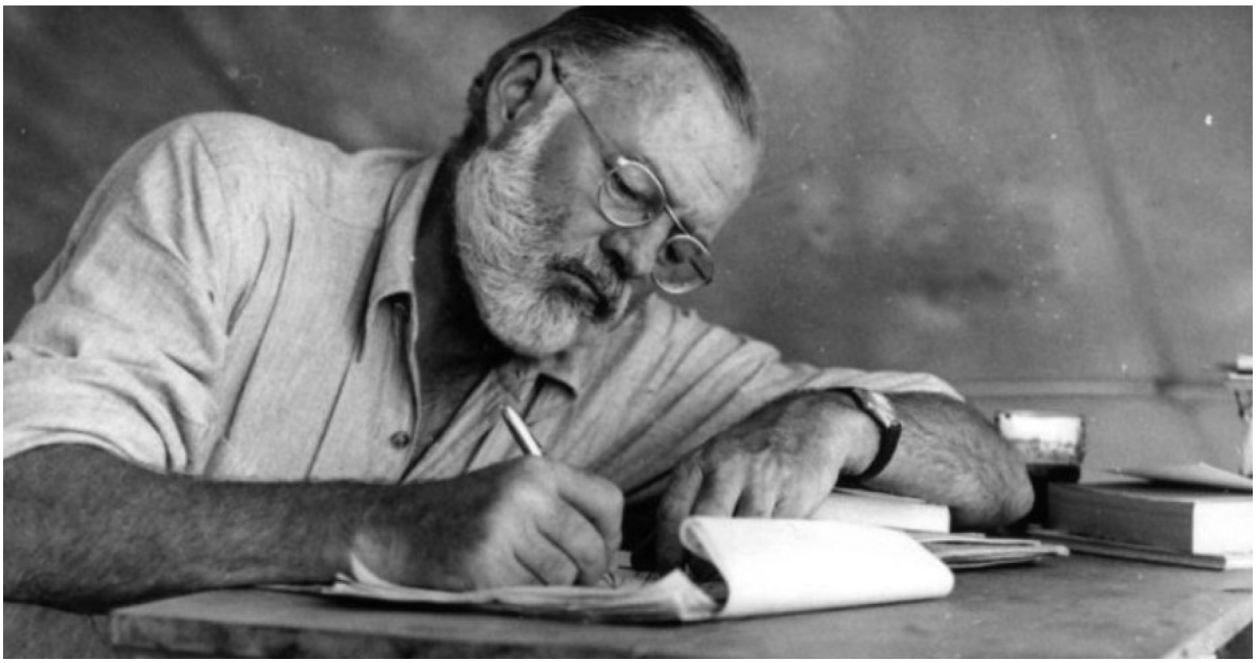

**Figure 1.** Ernest Hemingway writing at his desk, circa 1953. Courtesy the Ernest Hemingway Collection, John F. Kennedy Library, Boston. Hemingway lived in Cuba from 1939 to 1960 where he wrote *Islands in the Stream, The Old Man and the Sea, A Moveable Feast and For Whom the Bell Tolls.* In *A Moveable Feast* he wrote, "the only kind of writing is rewriting". This observation is especially important for physician authors as they rewrite their scientific papers to be "ever shorter, ever clearer". In 1954 Hemingway was awarded the Noble Prize in Literature.

The COVID pandemic brutally hit Cuba's economy and healthcare, diverting resources and stopping transplant programs in 2021. Moreover, there was double hit with a reinforced US economic embargo leading to further economic restrictions. Normal maintenance and repair of central services, the electrical grid and public services were left broken. Apheresis machines stopped for hours during collections due to technical problems; cell counting equipment failures forced late night counts in other hospitals; single leukapheresis runs in individuals became common due to the scarcity of disposable equipment; and conditioning regimens were revised due to the scarcity of drugs. Procedures taken for granted overseas had to be constantly reconsidered based on the availability of equipment and supplies.

How is all this managed? Several approaches are employed. We don't use cryopreservation, similar to other countries with restricted resources (*Bone Marrow Transplant,* January 2025). We use fresh cells cooled at 2-4°C with viability for 24-72 hours until infusion. Occasionally we alter preparative regimens according to drug availability. Accordingly, transplants have to be planned well in advance to allow sharing of resources,

**Figure 2.** Left, A symbol of resilience and resourcefulness, there are an estimated 60,000 vintage American cars in Cuba. This is a result of strict US export embargoes first placed in 1962. With restricted access to new American cars, finding parts and constant repairs are required to keep the old cars running. Right, Dr. Keith Sullivan, a visiting professor in 2024, shown at the wheel of a 1955 Buick Roadmaster.

**Figure 3.** Hurricane season lasts about six months in Cuba. *Hemingway's Hurricane* by Phil Scott details the deadly 1935 storm. Shown above, taping windows in Havana's HAH in 2019 hoping to strengthen the glass and protect from flying shards, albeit the proof of such benefit is limited.

intravenous sets and supportive care medicines across hospitals. Sometimes this gives the impression that performing a stem cell transplant is comparable to running an obstacle course, where you can only go forward and there is no choice but to overcome challenges along the way.

The support given by the Cuban Health System, which provides the antibiotics and drugs for the conditioning and posttransplant immunosuppression, has been essential as has been the solidarity of hematologists across the country. Individuals who volunteer when a specific resource is needed by our hospital; the timely advice of the most experienced colleagues, including the opinion of foreign experts linked to our service; and above all the will and constant effort of the involved teams. Such solidarity has allowed us to introduce haploidentical transplants (*Transplant Cell Ther,* February 2023), develop and standardize autologous HSCT in multiple myeloma (*Rev Cubana Med,* June 2024), and obtain encouraging results in Hodgkin's lymphoma *(Rev Cubana Med,* March 2021*)*.

Collaboration with overseas specialists has played an important role in these efforts for development of HSCT in our hospital (figure 4). This has allowed us to keep our professionals updated (figures 5 and 6) and submit joint publications describing our experience. Researchers from UIC in Chicago and HAH in Havana collaborated in retrospectively analyzing 101 consecutive patients with adult acute leukemia who received HSCT at HAH from 1986 to 2016. Of these, 82 had acute myeloid leukemia (AML) and 19 had acute lymphoblastic leukemia (ALL). Of the 82 patients with AML, 35 received an allogeneic (AML-allo) and 47 an autologous (AML-auto) HSCT. Overall survival (OS) was 34% in AML-allo and 38% in AML-auto, whereas the relapse-related mortality rates were 25% and 40%, respectively. Of the 19 patients with ALL, six received an allogeneic transplant with an OS of 33%. To our knowledge, this was the first scientific report on HSCT performed in adult patients with acute leukemia in Cuba (*JCO Global Oncol*, December 2018).

Overcoming economic restrictions is the story of individual physicians, staff members and, most of all, our patients who frequently demonstrate remarkable grace under pressure. There have been numerous experiences and various problems that we have had to face. Last year during leukapheresis of a myeloma patient, the only functioning apheresis machine (two others were unusable) stopped running. The technicians came shortly afterwards and were working on it for several hours. I cannot forget the astonished look of

**Figure 4.** Rounding on the Hematology Service, Hermanos Ameijeiras Hospital (HAH), September 2022.
From right to left: Damiano Rondelli (University of Illinois at Chicago, UIC), Chukwuemeka Uzoka (UIC), Calixto Hernandez (HAH) and the rest of UIC and Cuban teams.

**Figure 5.** Invited speakers at the 5th International Workshop on HSCT, October 12, 2024, Hotel Nacional de Cuba, Havana. From left to right: Matías Sánchez (University of Illinois at Chicago, UIC, USA), Sebastián Galeano (Hospital Británico, Uruguay), Ana M. Ávila (UIC, USA), Cristobal Frutos (Instituto de Previsión Social, Paraguay), Calixto Hernandez (Hospital Hermanos Ameijeiras, Cuba), Damiano Rondelli (UIC, USA), and Keith Sullivan (Duke University, USA).


**Figure 6.** An evening news TV screenshot of participants at the International Workshop on Stem Cell Transplant in Havana, October 12, 2024. Approximately 100 attendees from five HSCT centers across Cuba participated in the four-day training program sponsored, in part, by the American Society for Transplantation and Cellular Therapy, the Worldwide Network for Blood and Marrow Transplantation, the Cuban Society of Hematology, the Latin American Blood and Marrow Transplant Group, and the University of Illinois at Chicago.

the patient when they opened the machine from the rear exposing its internal mechanisms. It was almost unthinkable that after "disarmament" the procedure could be continued, but the repair was achieved and the leukapheresis concluded.

In the early 2000s, I was a young hematologist having just graduated. I remember an occasion in those early years when the hematology complex broke down (no others were then available in the city) and several patients with high-risk disease were awaiting transplant. In a meeting with the director of the hospital and members of the hematology staff, we were asked whether we could continue the transplants while only performing the hematocrit and checking the peripheral smear by microscope. We had no other good treatment options. So we said yes, proceed, and the three subsequent transplants were successful.

Another time when we were just restarting the program after COVID, we were presented with a patient from another Caribbean island who needed an autologous transplant but had several comorbidities including renal damage. We explained in detail our local difficulties, the other nearby countries with transplant capabilities and the risk factors involved with his transplant. I remember the immediate response when looking me straight in the eyes, he said, "I trust Cuba and its medicine—I will do it here". And so it was, and a few months later his transplant was performed without significant complications.

## AUTHOR PROFILE AND CONTRIBUTIONS TO THE FIELD

Calixto Hernandez Cruz is Professor of Hematology at the University of Medical Sciences in Havana. He was the Head of the Hematology at Hermanos Ameijeiras Hospital (HAH, 2011 to 2024) and more recently the Deputy Director for Teaching and Research at HAH. He is a member of the Cuban Hematology and Oncology Societies, a Board Member of the Latin American Bone Marrow Transplantation Group, and the Head of the Cuban National BMT program. He leads the National Hematology Group aimed at developing HSCT in Cuba and establishing international collaborations.

### *Damiano Rondelli*

About ten years ago the stem cell transplant program at the University of Illinois at Chicago

(UIC) began a collaboration with cell transplanters at HAH in Havana. It was still a time when Cuban physicians, who were highly recognized professionals, were allowed to visit the US under strict visa requirements for short-term training. In the 1980s, BMT in Cuba had been started at the HAH in Havana. The activity was always limited by several relevant factors: limited resources for diagnostics and supplies; limited supplies of standard drugs such as oral busulfan (which was produced locally) and granulocyte-colony stimulating factor; and limitation of allogeneic transplants to matched related donors since Cuba could not access the US-based National Marrow Donor Program for unrelated donors.

Involvement of UIC with Cuba began in 2015 when I was a last-minute invitee to a 4-day visit to Cuban healthcare institutions in Havana organized by my Department of Medicine. Our cardiologist had to drop out for personal reasons and I was the assigned substitute. Because of the late reassignment, there were no planned visits for me to their hematology or BMT wards. Upon my return home, Dr. Calixto Hernandez Cruz from their HSCT service contacted me since he heard of my visit and wanted to connect. He asked if he could spend some time in Chicago to learn how to select haploidentical donors and perform the procedure since that would be the only option for Cuban patients without a matched related donor. From the very beginning I learned a lot from Calixto, especially on how efficiency in Cuba meant something far different from efficacy. The most efficient strategies depend on "how to obtain the best results with the little resources that we have" vs "what is the most efficacious drug that unfortunately is not available".

An example was their policy in acute leukemia. For decades they had adopted the strategy that every adult acute leukemia patient would receive a stem cell transplant as consolidation therapy. If a matched related donor was available the patient would receive an allograft, and in the absence of a suitable related donor, an autologous transplant would be the consolidation treatment. This applied to all patients with acute myeloid leukemias and many with lymphoblastic leukemia when a cytogenetic profile was not available. Was this based on rigorous randomized studies? Of course not. But being unable to characterize the leukemia by cytogenetic or molecular testing, a high-dose chemotherapy regimen followed by stem cell rescue was a practice that had shown efficacy in large studies in intermediate risk AML and in ALL in the absence of maintenance therapy. More importantly, it was feasible in Cuba.

This conversation with Calixto led us to analyze the data with a huge effort of the team at HAH to find charts sometime a few decades old, and capture as much information as possible in 101 transplant recipients (*J Glob Oncol.* December 2018). After spending 2 months in Chicago, Calixto returned to Cuba and started the haploidentical transplant program following our protocols. Because of US political decisions, doctors from Cuba were not able to visit the US in the following years and our collaboration remained focused on building capacity through medical education to be provided in Cuba. Although it is a relatively small island, communication between different areas is limited, and patients often do not have the resources to move to another province for tertiary treatment. Thus, there are multiple small centers in Cuba performing autologous transplants. In contrast, allogeneic transplants are referred to Havana, either to a pediatric institution or to HAH for adults.

In October 2017 we jointly organized our "*1st Taller Internacional sobre Transplante de Progenitores Hematopoyeticos – CUBA-ESTADOS UNITOS*". This event gathered about 80 hematologists from several areas of Cuba with two important goals: 1) to give lectures on updated outcomes in BMT with protocols not yet available in Cuba, but of great interest for the local physicians who do not have the opportunity to attend international conferences; and 2) to have every Cuban center present their experience in BMT and have a discussion with us. From the first conference, it was a success and since 2017 has been repeated yearly except during the COVID pandemic. During the last meeting in October 2024, the venue was moved from HAH to the prestigious Hotel Nacional and the conference was covered by the national TV news channel (figures 5 and 6).

I find the collaboration with HAH and Dr. Calixto Hernandez extremely powerful as it has focused on how to help patients with our knowledge and their creativity, despite almost unsurmountable financial obstacles. So, when I brought some PICC lines or CVC kits in my suitcase it did not feel like anything special; just the way it is to make the best we can, with what is possible. Indeed, Global Health is the interstitial space to impact lives across languages, latitudes, culture, races, and governments. Human relationships grow in this context of grace under pressure to become stories of friendship, resilience and scientific advancement.

## AUTHOR PROFILE AND CONTRIBUTIONS TO THE FIELD

Damiano Rondelli is the Michael Reese Professor and Chief of Hematology and Director of BMT and Global Partnerships at the University of Illinois at Chicago (UIC). His clinical research focuses on transplant for myelofibrosis and sickle cell disease and the use of total marrow irradiation. In 2011 he started a global health initiative to build BMT capacity (*UIC GlobalBMT),* initially in Nepal then India, Ukraine, Cuba, Bolivia, Greece, Nigeria, Uganda and most recently at the Ramaiah Hospital, a non-profit university in Bangalore. In 2017, ASTCT established a Committee on International Affairs under Dr. Rondelli's leadership and he continues to increase access to BMT through the Worldwide Network for Blood and Marrow Transplantation. Since 2018, he has conducted a Training Course at UIC hosting 4-5 overseas physicians for 5 weeks each year.