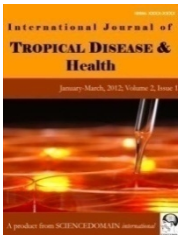

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Bone Marrow Transplantation to Cure Sickle Cell Disease using the Diffusion of Innovation Theoretical Model

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Author's contribution

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ABSTRACT

This project outlined use of the diffusion of innovations model to disseminate bone marrow transplantation technology for the cure of sickle cell anemia and other hemoglobinopathies. Besides, we Identified technologically developed nations that have the relevant medical workforce and infrastructures for BMT. Also discussed, is the necessity of equipping transplant facilities with the construction of the CLEAN ROOM with the state- of- the science resources to protect SCD patients from nosocomial infections. To save human lives and avoid unnecessary casualties, the medical team must protect their patients from hospital acquired infections (HAI), nosocomial and iatrogenic diseases during administration of transplant innovative device. Medical institutions must maintain continuity in sustainable, scientific workforce development. Finally, we explored the ethical, legal, social, and financial implications of adopting Bone Marrow Transplantation medical innovations to cure sickle cell anemia.

Keywords: Bone marrow transplantation; sickle cell disease; hemoglobinopathies; genetic disease burden; the clean room; graft versus host disease; the diffusion of innovation model; nosocomial infections.

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1. INTRODUCTION

The international scientific community and political administrators are aware of the importance of biomedical and engineering technology in alleviating the socio-economic hardship and disease burden in the developing nations worldwide. Research studies derived from genomics have revealed the cogent reason for the diffusion of medical and technological innovations to developing nations where there are chronic diseases and massive public health problems associated with ineffective and poorly developed medical infrastructure, inadequate workforce and underdeveloped technological resources. After the accomplishment of human genome sequencing, innovations from genomics have confirmed the application of bone marrow transplant (BMT) technology for the cure of sickle cell disease (SCD), cancer and other hemoglobinopathies. Researchers at the National Institutes of Health explained how sickle cell is caused from altered gene which produces abnormal hemoglobin, the protein in normal red blood cells which carries oxygen throughout the body. When exposed to low oxygen, red blood cells collapse into a crescent, half moon-shape and become stiff and sticky. Clumps of these cells impede blood flow and at this stage, the patients experience severe pain, organ damage, from lack of oxygen and stroke. Clinical observation reveals that anemia develops in most SCD patients because sickle cells die off quickly and bone marrow cannot make new ones to last like normal hemoglobin [1].

The West African areas of sub-Sahara Africa constitute the global epicenters of sickle cell disease. Also, the increased frequencies of SCD and other hemoglobinopathies are now diagnosed in Greece, India, Turkey, Iran, Saudi Arabia, Mediterranean basin, and many parts of Sub-Sahara Africa. Statistically, millions of SCD patients worldwide experience the excruciating complications of sickle cell disease. In the United States, sickle cell disease is the most common genetic disease and approximately 80,000 Americans have the disease. Sickle cell occurs in a frequency of one out of every 500 African American births and one in 100 Hispanic Americans carries the sickle cell trait. It has been estimated that about two million African Americans or one in twelve have sickle cell trait [1,2]. Paul Barton [3] has estimated the frequency of sickle cell in United Kingdom to be 20,000 and worldwide about two million manifesting the classical symptoms of sickle cell disease. He argues that for every one case of doubly homozygous, allelemorphic genes, there are three siblings who are carrier of some forms of hemoglobinopathies.

The use of Bone marrow transplantation (BMT) technology to cure sickle cell disease at the right time cannot be overstated. The prevalence of SCD and other hemoglobinopathies worldwide has become an international public health enigma. Globalization and rapid human migration activities have led to the proliferation and distribution of alleles of sickle hemoglobinopthies to numerous parts of the world. To a large extent, improvement in molecular gene probe and genetic analysis have also facilitated more efficacious detection of sickle cell genes in population groups previously presumed to be free from sickle hemoglobinopathies. Efforts to reduce the global prevalence of sickle cell disease must be targeted at the various international epicenters of these genetic diseases. Unfortunately, these are the developing and least developing nations which have ill-equipped medical infrastructures and underdeveloped technologically resourses. Since the least-developed and other developing nations are currently faced with massive disease burden even in the twenty-first century, the study described here was designed to:

- Outline use of the diffusion of innovations model to disseminate bone marrow transplantation technology for the treatment of sickle cell disease and other hemoglobinopathies.

- Identify technologically developed nations having the relevant medical workforce and technological infrastructure for BMT.
- Accentuate the relevance of equipping transplant facilities with the construction of the CLEAN ROOM with the state of the science resources to protect SCD patients from nosocomial infections and iatrogenic diseases.
- Discuss the importance of reducing or practically eliminating of hospital acquired infections (HAI) and other nosocomial and iatrogenic diseases during BMT procedure.
- Discuss capacity building, and scientific workforce development.
- Explore the ethical, legal, social, and financial implications of adopting Bone Marrow Transplantation medical innovations to cure sickle cell anemia.

2. DIFFUSION OF MEDICAL INNOVATION TO CURE SICKLE ANEMIA

Everett Rogers [4], a professor of rural sociology developed and advanced the concept of Diffusion of Innovation in 1962. He argued that diffusion is the process by which innovation is communicated through certain channels over time among members of a social system. For over one-half of a century, the genesis and origin of diffusion of innovation are varied and span across multiple disciplines such as sociology, marketing, social network analysis, demography, epidemiology, medical sciences, and positivism and computer sciences among others.

The theoretical construct was conceptualized by Everett M. Rogers [4] as the diffusion of innovation. This model involves the Bell-shaped curve and the various adopter categories. The diffusion theory provides succinct explanation for the diffusion of innovations in populations. Genomic applications regarding bone marrow transplantation involve innovations that have not been made ubiquitous in the developing and least developed nations. Rogers[4] efficiently categorized adopters based on when they adopt innovations. They consist of innovators, early adopters, early or late majority and the laggards. The rate at which they assimilate innovations was depicted by the perfect bell-shaped curved with -3stadard deviation to +3standard deviation [Fig.1].

Innovators are the first to adopt an innovation. The second group consists of the early adopters. This group is very interested in innovations, but they do not want to be the first involved. This category is where we find very progressive developing nations that have appreciated the benefits of research derived from bone marrow transplantation to cure sickle cell anemia and other hemoglobinopathies. They continue to invest their resources to translate both theories and intellectual vision into practical realities. Early adopters are respected by others in the social system and perceived as opinion leaders. The next group is the early majority. This cohort of nations includes those in many of the developing nations who are interested in innovative bone marrow transplantation, but do not have the financial capital and the competent workforce to participate in innovative medical ventures. They may be interested in innovation but will need external motivation to get involved in such innovative activities. The Late majorities are comprised of nations that have the resources but are very skeptical and will not adopt an innovation until other nations have tried and possibly succeeded in innovative activities. The last group is characterized as the laggards. The Laggards are usually the last people to get involved in any innovation. In this model, most of the least-developing nations may never get involved in innovative genomics; they lack the resources and the motivation even if they ever get involved at all. They may cite ethical, religious, cultural and socio-psychological nuances for their inertia [4, 5, 6].

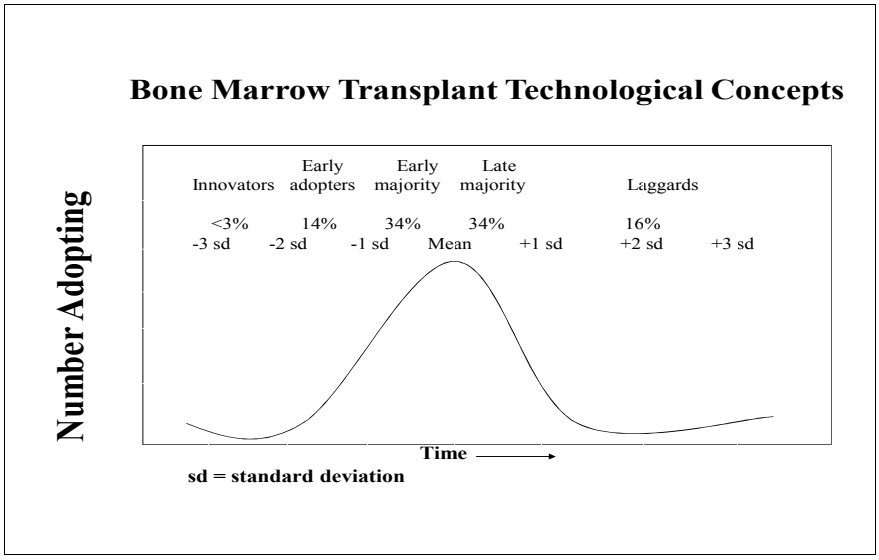

Fig. 1. Diffusion of innovations derived from the bell-shaped curve and the adopter categories

Legends:
Innovators- *are the first cohort to adopt an innovation. This category of people usually wants to be the first to do something.*
Early Adopters*- Involve the category of people who are always very interested in innovation but they do not want to be the first to get involved.*
Early Majority*- This category of people may be interested in innovation, but will need external motivation to get involved.*
Late Majority*- This category of people may be interested in innovation but usually skeptical, suspicious and will not adopt innovation until most people in the social system have done so.*
The Laggards*- This category of people is the last group to get involved, if they get involved at all (They may never get involved).*

Roger [4] later identified the five stages required for innovation to occur in his later editions of the Diffusion of Innovations to include knowledge, persuasion, decision, implementation, and confirmation. Therefore, medical administrators, clinicians and behavioral scientists must be provided succinct information about bone marrow transplantation technology and the requisite caveats. At the persuasion phase, administrators must be provided copious information about BMT technology and other detailed account about the relevant precautions. At the decision stage, the team takes the concept of BMT technology and weighs the advantages and disadvantages of using BMT to cure sickle cell disease and whether to adopt or reject the innovation. At the implementation stage, the medical team could at that time employ the innovation to a varying degree such as systematically implementing sickle cell BMT. Initially, at the tertiary health care centers in the developing nations, the medical workforce might implement BMT procure before disseminating this intervention to the general hospitals. At the confirmation stage, the medical administrators and other political leaders are in position to continue adoption and use of BMT technology in well-furnished hospitals nationwide [4]. These stages are currently being anticipated in the diffusion of BMT technology and other key components of innovative genomic medical interventions in Africa and other developing areas of the world.

3. ADVANCED NATIONAL AND INTERNATIONAL MEDICAL CENTRE

The G-8 nations constitute the global geographical regions where BMT technology and other innovative medical interventions are currently being implemented. In the age of genomic medicine, they constitute the innovators. They have the financial capital; they have the scientific and technical workforce, and the high-technological resources for sequencing and the construction of scientific clean rooms for the clinical procedure performed on bone marrow transplant patients.

Scientists and clinical researchers at NIH have led pioneering efforts in the translations of BMT technology to bedside medicine. Between 1991-1995, the scientists and clinicians who have been involved in the collaborative study group that enrolled patients for the medical procedure, after they were provided the requisite counseling include parents of patients with SCD; consist of medical institutions such as Emory University, Atlanta, The Dana Farba Institute, George Washington University, Washington DC; Howard University, Washington, Washington, DC; The Children Hospital, Harvard University Medical Center, The Boston Comprehensive Sickle Cell Center, Boston MA, University of North Carolina, Chapel Hill, NC; University of Texas, Dallas and Houston TX; Duke University, Durham; Indiana University School of Medicine, Indianapolis, Indiana; Stanford university; California; University of Southern California, Los Angeles, California; University of California, San Francisco, California; Medical College of Wisconsin and children's Hospital of Wisconsin, Milwaukee, Wisconsin; Yale University; Connecticut; Children Hospital of Oakland; Oakland University of Pennsylvania, Philadelphia; University of South Florida, Saint Petersburg, Florida; Saint Louis University Saint Louis Missouri; Fred Hutchinson Cancer Research Center and the University of Washington, Seattle; Washington; USA [1].

Recently, there were few medical centres that joined the collaborative study and they include medical centres in New York City, New York; University of Chicago Medical School, Chicago Illinois; University of Illinois Medical Center, Chicago Illinois; Tulane University Medical Center, Sickle Cell Centre of Southern Louisiana, Louisiana and other medical institutions at Miami; Gainesville, Florida, Brooklyn, New York; Hackensack, New Jersey, Shreveport, Louisiana; Denver and Pittsburg, Pennsylvania [1, 2]

4. INTERNATIONAL CLINICAL CENTRES

The other international participating centers include; the University of Bonn, Augustin, Germany; Birmingham Children's Hospital National Health Service Trust, Birmingham, United Kingdom; The Hospital Henri Mondor, Creteil, France; Royal Postgraduate Medical School, London, United kingdom; and Hospital for the sick Children Toronto, Canada [1]

4.1 BMT in Developing Nations

Developing nations which currently have bone marrow transplant technical expertise and technological infrastructures include: University of Campinas, Sao Paolo, Brazil; Mexico, Jordan, Turkey, India, and South Korea. These countries currently have the state of the art comprehensive medical facilities and highly competent medical and clinical team that have facilitated the scientific breakthrough and accomplishment of these nations. Based on Roger's(2003) conceptualization, principally, the G-8 are the innovators, and the early adopters' are the progressive developing nations such as Brazil, China, Korea, Jordan, India and South Korea among others.

4.2 Bone Marrow Transplantation Technology

Bone marrow transplant is clinically described as hematopoietic stem cell transplant. The bone marrow is a soft spongy area in the centre of most human bones. The marrow produces different cells which are the key component of the blood and the marrow produces both white and red blood cells and the platelets. The white blood cells are used to ward off incipient infections while the red blood cell circulate and supplies oxygen to all parts of the body. All these cells develop from precursor cell within the blood described as hematopoietic stem cell[7]. There are three crucial transplantation techniques which are routinely used for sickle cell disease. They include “allogeneic” BMT or “syngeneic” haplo-transplant. Regarding the allogeneic BMT, this is the situation when the bone marrow is from a donor whereas it is syngeneic if the donor is an identical twin. In an allogeneic BMT, the new bone marrow infused into the patient must match the genetic make-up of the donor. In matched unrelated donor, it becomes crucial if perfect matched siblings are not found. With sickle cell disease, finding a matched donor from the transplant registries throughout the world is extremely rare. Medical scientists have also reported how patients without matched family or unrelated donors could benefit from haplo-identical mother-to child transplantation, which has shown encouraging results. However, this procedure is still at experimental phase.

The National Institutes of Health [2] specifically recommends carefully destroying the bone marrow of patients with SCD. Besides, they undergo a regimen in which their bone marrows are completely destroyed with chemotherapy. For the young under the age of 10, this treatment is appropriate, but for adult patients, the regimen is extremely toxic because, as a result of years of accumulated organ damage from the signs and symptoms of SCD, they are less likely to tolerate complete marrow transplantation. To achieve the process of curing SCD patients, the clinicians apply a low dose of radiation to the whole body. Two drugs, Alemtuzumab and Sirolimus are used clinically to suppress the immune system. On the one hand, Alemtuzumab depletes the patient’s immune cells, but does not adversely affect the blood stem cells. On the other hand, Sirolimus does not block the activation of immune cells but inhibits their proliferation, creating a balance that potentially assists in preventing rejection of the new stem cells [2]. In many other settings cyclosporine is used to suppress the immune system, preventing GVHS post transplant and Alentuzumab and Sirolimus are used for specific transplant. However, when allogeneic graft starts to proliferate in the recipient, an immunological graft versus-host reaction GVHD may occur. GVHD can affect one or more organs to varying degrees, with the most frequently affected being the skin, gastrointestinal tract, and liver. GVHD is a serious complication of BMT and can be fatal, therefore the prophylactic administration of cyclosporine (an immunosuppressive drug) is an important part of the pre-transplant and post-transplant treatment. Three or four doses of methotrexate may also be given in addition to cyclosporine during the first 15 days after transplant procedure.

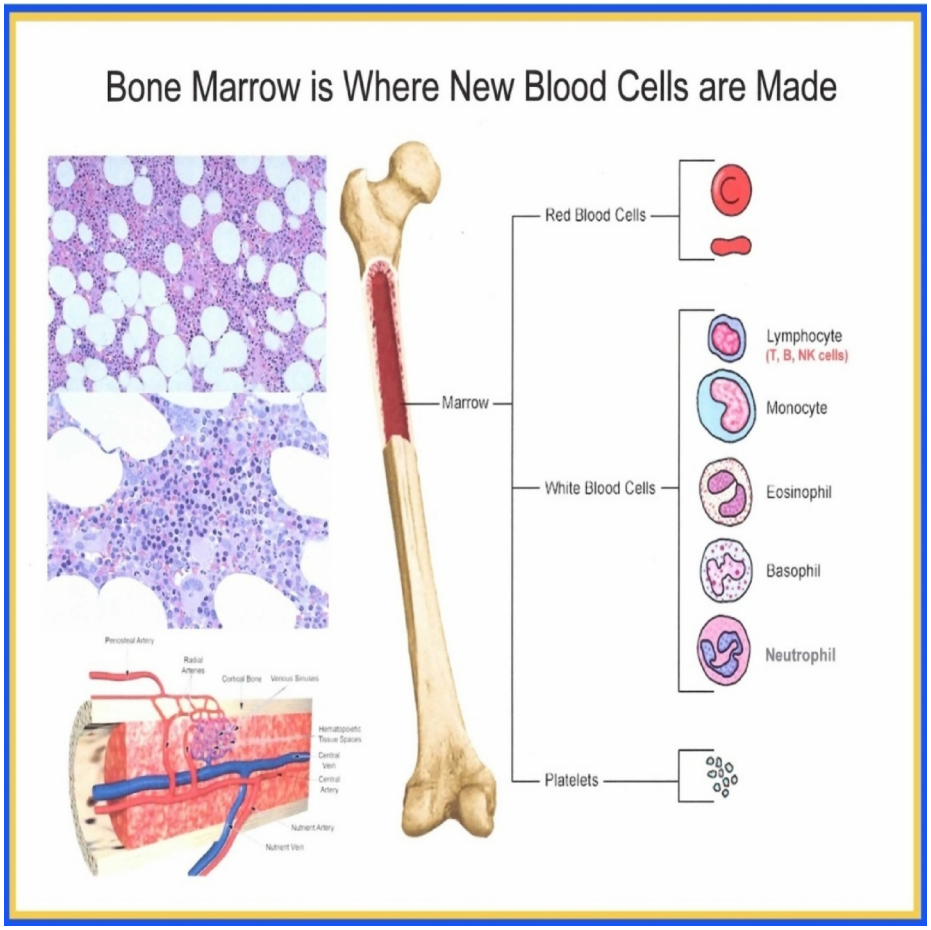

Fig. 2. Bone marrow where the new blood cells are made

Legends: *1. Lymphocytes are small white blood cells that play crucial role in the body's immune response. Lymphocytes enable the immune systems to ward off incipient stages of disease 2. Monocytes are mononuclear, phagocyte leukocyte. Monocytes are types of white blood cells. They are produced in the bone marrow and after about four days are released into the blood stream. They assist the body in fighting infections 3. Eosinophil is a granula leukocyte with a nucleus which has two lobes connected by chromatin and cytoplasm. They are also types of white blood cells produced in the bone marrow 4. Basophil is a granular leukocyte with an irregular shape, relatively pale-staining nucleus that is partially constricted into two lobes and a cytoplasm containing coarse bluish black granules of variable size 5. Neutrophil are types of white blood cells; they are produced in the bone marrow and they circulate in the blood[5,6,7].*

Based on the intervention at the NIH, radiation conditions the bone marrow, where donor stem cells move in and initiates the production of new, healthy red blood cells. Within a period of about two and one half years follow-up, the successfully transplanted children are alive, and sickle cell has been completely eliminated in nine out the ten children[2]. So far the NIH research team has successfully transplanted more than 25 patients without the occurrence of any graft versus host disease (GVHD). Their unique and scientifically designed room with air filters coupled with their technique in which their patients do not experience a prolong period with suppressed healthy immune status practically reduces the

risk of infections, and other hospital acquired infections (HAI) and ventilator acquired pneumonia (VAP). Their regimen is so unique that it could be performed in technologically resource challenged nations such as Ghana, Nigeria, Republic of Benin and Beirut among other epicenters of SCD and other hemoglobinopathies [2].

The American Society for Blood and Marrow Transplantation [8] reported guidelines for preventing infectious complications among Hematopoietic Cell Transplantation (HCT) recipients. Based on their guidelines, HCT was "defined as transplantation of any blood-or marrow derived hematopoietic stem cells (HSCs), regardless of transplant type- which includes allogeneic or autologous, or cell source peripheral blood [PB] or umbilical cord blood [UCB]" [8]). An in-depth analysis of cord blood transplantation is beyond the focus of this project. Ebomoyi and Cherry [9] laid the foundation for cord blood neonatal screening for SCD at the Tulane pediatric center in the early nineties but not cord blood transplantation.

5. CONTROL OF HOSPITAL ACQUIRED INFECTIONS AND INSTALLATION OF THE CLEAN ROOM

Hospital-Acquired Pneumonia (HAP) has been defined as pneumonia which occurs just 48 hours after a patient has been admitted into the hospital. Regarding the ventilator-acquired pneumonia, this is the variant of pneumonia which is diagnosed in patients more than 48 hours after endotracheal intubation [10. Microbiologists and other clinicians maintain that HAP, VAP are infections which could occur due to micro-aspiration of contaminated oropharyngeal secretions. As a result of the weakened immune status of SCD patients, concerted efforts must be made to protect the BMT recipient from HAP and HAI among other infections. Even among many other hospitalized patients, micro aspiration is usually a common source of infection occurring in over 50% of normal sleeping subjects and 70% of patients who are sedated or in depressed consciousness. Besides, micro aspiration in hospitalized patient is more virulent and more pathogenic because of the oropharyngeal secretions aspirated which are more likely to contain a wide variety of organisms that are not present under normal circumstance. In many SCD patients, the gram-negative bacteria account for 55% to 85% of HAP infections and gram-positive cocci account for 20% to 30% [10].

These infections are among the leading causes of preventable death in United States. By 2002, infections from HAP and VAP accounted for an estimated 1.7 million infections and 99,000 associated death in United States. Also, in U.S the mortality and morbidity caused by HAI, and the financial burden attributed to such infections has estimated to be between $28 to $33 billion. This amount escalates the annual health care cost in United States[1,2]. From our observations, patients with cardiovascular disease, cancer, sickle hemoglobinopathies, lupus and other chronic and degenerative diseases have weakened immune system that expose them to these deadly pathogens which invade their blood stream killing over 30,000 patients annually.

5.1 Innovative Medical Device "The DualCap" Intervention

DualCap is the most recently invented medical technique to eliminate deadly pathogens associated catheter insertion in most patients worldwide. DualCap is a sterile, single-use device which contains two disinfecting caps. One of the caps is for the needleless injection site (NIS), and the other is at the end of the intravenous IV tubing. Each cap contains 70% isopropyl alcohol and a patent-pending delivery mechanism. DualCap has been

demonstrated to significantly reduce the bacterial contamination which usually overwhelms recuperating patients worldwide. This innovative technology has been reported to prevent intraluminal contamination which is one of the ways that IV connectors contribute to catheter related blood stream infections (CRBSIs) which are among the leading causes of death in United States. In United States alone, over 500,000 patients die from CRBSI infections annually [2].

6. THE CLEAN ROOM

Bone marrow transplant for sickle cell disease necessitates the installation of the clean room, at least, in the ante-room before the medical team initiates the transplant procedure in the theatre where patients receive their bone marrow transplant. In the developing and least-developing nations, installation of the clean room can minimize the risk of hospital-acquired infections in convalescent patients.

Clinical epidemiological assessment of SCD has indicated the prevalence of a broad spectrum of infections which are life threatening with several organs in the body being principally damaged. In the kidney, there are the enuresis, hematuria, nephrotic syndrome, and urinary frequency among others. At the spleen, there is increased splenic sequestration crisis and abdominal pain. In the lungs, there is pneumonia and acute chest pain and in the bones, there is the onset of aseptic necrosis. Owing to poor oxygen circulation to the brain, stroke could occur with periodic headache. Leg ulcers could erupt on the skin and priapism is a major dysfunction in many male patients who suffer from sickle cell disease. In the eyes, sickle cell retinopathy and glaucoma are routinely observed while hepatomegaly, cholelithiasis and jaundice could occur at the liver [11,12,13, 14]. Depending on the variant of sickle hemoglobinopathies, different infections occur in different patients. These infections continue to weaken the immune status of most SCD patients, therefore without the clean room and comprehensive clinical strategies to eliminate HAI, iatrogenic and other nosocomial infections, the diffusion and dissemination of innovative BMT technology to developing and the least-developed nations could constitute medical suicide for unsuspecting clients who are already at the throes of compromised physical, emotional and psychosocial health status.

The installation of clean room in any developing or the least developed nations must involve engineers, molecular scientists, physicians, hospital epidemiologists, and the medical, pharmaceutic scientists, hospital administrators, management engineers and competent architects and building designers to develop specifications that can suitably meet the peculiar needs of nations that are confronted with extreme heat in the summer months and other environmental conditions which are unique to these nations.

By far most crucial is the problem of underdeveloped technological infrastructures such as erratic energy and unreliable supply of electricity, unreliable water supply, and the availability of relevant medical inputs and pharmaceutical products. Facilities in a medical clean room must not be compromised, because any sordid environment could result in fetal consequences for the patients. The medical clean room is a controlled and efficiently sanitized environment where products are prepared for performing BMT procedure. It is in the clinical room that the concentrations of airborne particles are controlled to specified limits. From epidemiological perspectives, interdisciplinary efforts are required to eliminate sub-micron airborne contaminants in the clean room; contaminants from visitors, health care workers, hospital facilities and equipment are constantly removed. The most frequently adhered to standards are those stipulated by the USA, Federal Standard 209E. Very strict

rules and procedures are adhered to to prevent contamination and infection of patients and the donor.

With Permission and Courtesy of Terra universal, Inc 2012, clean room equipment.

Fig. 3. The clean room equipment

Legend: *The clean room installed in the ante-room is where the clinical team wear protective gowns to protect patients from numerous hospital acquired infections which could compromise the health status of BMT patient*

Clean room panels by their design, promote aseptic processing. There are steel and plastic clean rooms. For any developing nation, installation of clean room must not compromise the health status of patients. Steel clean rooms are designed to eliminate or significantly reduce contaminants. There are five major sources: 1) facilities such as walls, floors and ceilings, paint and coatings, construction materials such as sheet rock or saw dust, debris from air conditioning, contaminated room air and vapors, spills and leaks 2) humans, their skin flakes and oil, cosmetics and perfume, spittle, clothing debris and hair 3) tool generated friction and wear particles, lubricants and emissions, vibrations, brooms, mops and dusters, 4) particulates in floating air, gram positive and gram negative organisms, organics and moisture floor finishes or coatings, cleaning chemicals, plasticizers(outglasses) and deionzed water and 5) products which are generated such as silicon chips, quartz flakes, clean room debris and aluminum particles [11,12,].

In steel clean room, the installed panels usually support aseptic operations. The panel material consists of powder-coated steel, 304/316 stainless steel, and tempered safety glass which meet the standard for disinfectants. The panels seams are caulked to meet USA,

FDA-approved silicone sealant to eliminate cracks which could be the habitat for agents of diseases and other contaminants [11,12].

In an effort to maximize contamination control, the high efficiency particulate air filters (HEPA) are installed in anterooms to maintain contamination control. HEPA can easily filter particles as tiny as 0.3 microns with a 99.97% minimum particle-collective efficiency. Clean rooms-architecture are designed to achieve and maintain airflow along parallel flow lines; this process is called laminar flow. Cleaning the clean room requires use of additional filtration, and well-trained cleaners. The sublime features of the clean room should constitute a detailed in-service training-course and the orientation of environmental health/sanitation staff in developing nations where the introduction of innovative BMT technology require trained sanitary engineers with unique and appropriate expertise.

The installation of clean room is required in the diffusion of innovative medical cure and treatment of patients with SCD. The training of physicians and other clinical workforce can also enable this diffusion of innovative technology to be accomplished. At many of the epicenters of SCD such as Nigeria, where SCD kills 100,000 infants every year, without universal screening and the management of the disease with penicillin prophylaxis, the diffusion of innovative BMT transplant technology cannot be safely implemented. However, the inadequate medical workforce is a major handicap; under-developed technology and lack of well-equipped clean rooms have compelled the sickle cell foundation of Nigeria (SCFN) to solicit assistance of the Mediterranean Institute of Hematology (IME) in Italy. This kind gesture led to scheduling of twenty Nigerian sickle cell anemia patients for BMT to cure SCD in Italy [13].

6.1 Capacity Building and Scientific Workforce Development

The premise for the efficient development of a collaborative scientific workforce is the sophisticated level of technological resources required for accomplishing BMT. Concerted efforts are required to sponsor and train physicians hematologists, clinical epidemiologists, modern genome epidemiologists, immunologists, medical microbiologist, virologist, and related behavioral scientists.

To illustrate, meaningful capacity building in BMT technology necessitates the mutual and on-going collaboration of medical clinical geneticists(MD; Ph.D.), obstetric and gynecologists(M.D), medical social workers, molecular epidemiologists(Ph.D.), clinical laboratory technologists, hematologists, maternal and child health specialists, pediatricians(M.D), pediatric nurses, health educators and basic research epidemiologists(Ph.D.). Genetic screening program could be a key component of the federal and state offices of public health with linkages to federal and state universities. The screening could be under the leadership of a microbiologist or geneticists. Follow-up genetic services can be coordinated at that level. Pediatric hematologists could serve as the director of the sickle cell clinic or as a member of the taskforce. Molecular epidemiologists have major role to play in assessing accuracy of numerous test in terms of sensitivity, specificity, clinical validity, analytical validity and the efficiency of test results and the cost benefits and cost-effectiveness of such state and national programs. The type of genetic services required is technically described as ”proband services.” When a genetic disease occurs, the family of the affected person (proband) wants to know the likelihood of occurrence with another pregnancy. The clinical geneticist will take medical history and construct a pedigree including as many generations as possible, examine the child, order necessary tests (cytogenetic and DNA analysis), recognizing specific syndrome features and hopefully

identify a disease syndrome. The department of obstetrics and genecology in collaboration with hematologists can establish birth registries for newborns with SCD and other hemoglobinopathies and alert parents about the availability of BMT technology for parents who are interested in this innovative medical procedure.

6.2 Ethical, Legal, Social, and Financial Implications of BMT to Cure Sickle Cell Disease

With SCD being recognized as a genetic disease of global public health significance, there is the moral imperative to utilize the existing technology to cure the disease. Compliance with ethical medical standards demands that comprehensive health counseling of the donor and recipient of BMT is integrated into the medical procedure so as to alley the anxiety and fear associated with this relatively risky procedure. To reiterate, there are three different techniques for conducting BMT which are dependent on whether the donor is a perfect match. They include the autologous BMT, the allogeneic and haplo-BMT. A detailed analysis of cord blood transplant is beyond the scope of this project.

Clinical epidemiological studies have revealed the exposure of most BMT patients to a broad spectrum of physical, social and emotional dysfunctions. Therefore, it is ethically imperative that the medical team involved in BMT fills out and obtain the relevant approval of the Institutional Review Board (IRB) before enrolling SCD patients in their innovative medical intervention. All patients must be informed about risk of graft versus host disease (GVHD), the possibility of delayed fertility or potential sterility and other associated health issues. Since patients are required to stay in the hospital between five to eight weeks, their protection from HAI, nosocomial infections and iatrogenic infections is extremely crucial. In many of the developing nations, innovative medical devices such as the dual cap, installation of the clean room have not been disseminated to their national state and local medical centers. Besides, their workforce who has not been trained in modern genomic medicine poses clinical challenges to the survival of BMT patients.

6.3 Legal Implications

In the industrialized nations, a medical practitioner is liable for his/her actions. The law is that “tort-negligence” by the physician is punishable by pecuniary damages. Also, if the case of negligence is legally proved, the physician may be subjected to criminal liability. Medical practitioners owe special allegiance to their patients by abiding by the Hippocratic Oath “to do no harm” to any patient [14].

However, regarding this innovative medical intervention, the approval of BMT procedure does not completely negate the risks reported about the intervention. With the documented myriad complications associated with BMT, the legal ramifications are such that when certain casualties occur, the law examines situations, underlying conditions whereby the incidence could have been prevented or avoided. The medical practitioner may not be held accountable but only that they practice medicine prudently [14, 15].

The medical workforces including other scientists are liable to “intentional torts” for such actions as defamation of patients’ character from access to patients’ confidential medical records, intentionally inflicting psychosocial agonizing distress on their BMT patients. Empirical research studies have revealed considerable interest by most adult sickle cell patients in potentially curative treatment using BMT, in spite of the documented risk of

treatment-related death. There are vagaries about lack of agreement between physicians' recommendation and patients' attitudes [16]. Kodish et al. [17]) have surmised that "Patient may not think about risks and benefits the way doctors do" Most patients are most likely to sway their decision only when there is an in-depth counseling regarding BMT procedure from a competent modern genome epidemiologist.

The ethical quagmire is whether the physicians should discuss transplantation with their patients, even though they may not feel that it is an appropriate procedure for specific patient? Most epidemiologists, hematologists, medical sociologists and health educators believe that physicians on transparent ethical grounds should provide appropriate information and succinct health education about all treatment alternatives in a way that enhances patient autonomy and rational decision making process. This is perceived as one of the fundamental duties of the
physician [18].

6.4 Social Implications

The major social implications of BMT in developing nations pertain to training competent workforce, establishing well equipped clinical centers and training physicians with expertise in hematology, immunology, molecular genetics, modern human genome epidemiology, health education, oncology and other behavioral sciences area. Massimo [18] has emphasized that it is unethical for any trial to be performed at any center such as those in many of the Sub-Sahara African nations without sufficient expertise, simply by fiat of "last hope." The use of penicillin prophylaxis, folic acid and other palliative treatment are other available options for many patients. Annas [19] has been vociferous about patient's rights to information. According to him, the right to information includes the right to be made aware about reasonable alternative treatments, including research protocols which are relevant to the patient's condition. Brunet-Jailly [20] also corroborates the position of Annas (1998) by emphasizing, even if the treatment choice of the patient may not be in accordance with the physician's recommendations, competent autonomous decisions should be honored because the patient's autonomy and dignity should be respected and medical paternalism should be avoided under any circumstance [19,20]. In many of the industrialized nations where Ethics Committee of the medical institutions already exist, the minor, parents of SCD patient must be informed about the use of anesthesia for sibling donor and the discomfort associated with such procedure. In compliance with the guidelines of the ethics committee, voluntary donor's consent is required at different stages of the planned BMT procedure which occur, at entry in the registry, when typing of the major histo-compatibility complex, and at bone marrow harvesting under general anesthesia. In many of the progressive developing nations intending to set-up such BMT center, compliance with these ethical guidelines is very crucial for successful bone marrow transplantation for the unsuspecting clients.

6.5 Financial Implications

The diffusion of this innovative BMT technology is frost with unaffordable financial constraints. Even in the affluent G-8 nations, the integration of BMT into bedside medicine is basically at experimental phase. This innovative procedure is extremely expensive and it poses financial challenges to medical administrators in resource-starved developing nations. The progressive developing nations that have established outstanding BMT centers have utilized government financial support for constructing and furnishing their centers with the

state- of-the- art medical infrastructures. These nations include Mexico in North America, Jordan and Turkey in West Asia, India in South East Asia and South Korea in East Asia.

The crucial lesion of this project is to sensitize the medical community and political administrators in the developing nations about the significant breakthrough involving research derived from genomic science. We have also emphasized the relevant strategies to harness such scientific benefits without jeopardizing the lives of children in society where over 100,000 children are born each year in Nigeria alone with sickle cell and other hemoglobinopathies. We hope this project will alert, the World Health Organization (WHO), the United Nations Children Emergency Fund (UNICEF), Clinton Global Initiative and other international organizations, including the federal, state and local governments of developing nations about the need to financially support the establishment of BMT centers so as to alleviate the pain and suffering of numerous sickle cell disease patients worldwide.

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COMPETING INTERESTS

Author has declared no competing interests.

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