

# CHAPTER 3

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### **3 Stem cell research engenders interdisciplinary collaboration in science, ethics and religion:**

#### RECONCILING SCIENTIFIC PROGRESS WITH CULTURAL PRACTICES AND RELIGIOUS BELIEFS

Science has the potential to impact significantly on society, and the South African Government's drive towards a knowledge-based economy aims to harness this potential. One example of particular interest is the field of stem cells. Although the field is likely to have a significant impact on healthcare, it is intrinsically fragile. This fragility results from the convergence of science, ethics and religion around issues such as the origin of life (in the case of embryonic stem cells). In addition, there is lack of concordance between the rapid rate of technological innovation on the one hand and the implementation of appropriate legislation on the other. Appropriately focussed inter-disciplinary collaborations considering science's impact on society, are necessary to avoid the negative consequences of this fragility. The joint conference co-hosted by the Vatican and NeoStem, an American-based international biopharmaceutical company, in Rome in November 2011, is an important step in this direction.

Stem cells are the building blocks from which all the different cells of the body are derived in response to a finely orchestrated series of chemical and mechanical signals. Stem cells have been used successfully for several decades to treat patients with a variety of diseases, and their future potential as therapeutic agents has opened up an exciting new field in medicine. In order to harness the full potential of the rapidly growing field of stem cells, it is important for the diverse disciplines implicated therein to align their goals and values. Stem cells and their application in "personalised medicine" extend far beyond the disciplines of medicine and pharmacology. There are humanitarian, social, ethical and religious concerns that will arise from developments in this field, and to ignore their impact on our communities would be to the detriment of all concerned. The establishment of interdisciplinary networks is necessary in order to retain and even accelerate the current momentum of research and to ensure that therapeutic benefits and patient safety are maximized.

The seemingly unorthodox collaboration between the Vatican and NeoStem is an example of the type of interaction between religion, science, medicine, bioethics, economics and philosophy that could pave the way for an interdisciplinary approach to stem-cell research.

Their unusual collaboration made headlines last year when the Vatican donated \$1-million to NeoStem's Stem for Life foundation, the objective of which was to develop 'ethical stem cell research'. The worlds of science and religion do not necessarily oppose each other *per se*, the Vatican has not been seen as an unbiased partner with regard to support for science, since it will be recalled that the Vatican condemned Galileo Galilei as a heretic for his theories on the universe. Rev. Tomasz Trafny, a Polish-born priest, gave the LA times (20 October, 2011) two reasons for the Vatican's interest in collaborating with NeoStem:

First, they [NeoStem] have a strong interest in ... searching for the cultural impact of their own work, which is very unusual. Many companies will look at the profit and only at the profit. And the second, of course, is that they share the same moral, ethical sensitivity.... Because of that ethical position, we entered into this unique collaboration.

NeoStem has interests in adult cellular regenerative therapy, both in harvesting and storing adult cell units as well as in manufacturing adult stem cell (ASC) therapeutics. At first glance, there are no specific qualities that distinguish NeoStem from other players in the ASC therapy field. Although Neostem's interaction with the Vatican has met with some opposition, credit needs to be given for their creative approach to bridging the divide across disciplines. The reasons for NeoStem's collaboration may differ from those espoused by the Vatican. For example, there might be more to gain for NeoStem in the collaboration from a commercial perspective than the Vatican cares to admit. However, the collaboration was showcased under principles of morality and ethics, and although NeoStem will almost certainly benefit commercially, the focus was nonetheless on how to make stem cell therapies more ethical by focusing on ASCs rather than embryonic stem cells (ESCs).

The most widely publicized moral opposition to the use of stem cells comes from the use of ESCs. The Vatican's stance against the destruction of human embryos for the production of ESC therapies made them the perfect partner for NeoStem's ASC campaign. The Vatican is of the opinion that destroying an embryo does not uphold the ethics that maintain respect for life, regardless of the stage of the embryo's development (Pope Benedict XVI, 2006) and therefore gladly support NeoStem's alternative 'ethical stem cell research' which is limited to ASCs. Public awareness of ASCs is very limited to say the least, and their potential future applications are not well understood.

The Vatican-NeoStem conference strongly promoted the potential therapeutic applications of ASCs and the impact that cell-based therapy will have on society's social, cultural and religious interactions. A limited number of new insights were offered at the conference, at which various kinds of ASCs and their potential therapeutic applications were presented as better 'ethical alternatives' to ESC therapies. Current misconceptions regarding ASCs were discussed, together with patient testimonials that highlighted several successes in ASC therapies. Speakers strongly contrasted the apparent moral and ethical high ground of ASC therapies to that of ESCs. Reasons for the Catholic church's support for ASCs were given from a theological, philosophical and humanitarian point of view, with emphasis on the moral and ethical responsibility that scientists have towards society. In short, the public platform created by the conference was cleverly utilised to convey the scientific message of "adult stem cell hope" (inevitably mixed though with a little "stem cell hype" – specifically where patient testimonials were used to underscore the effectiveness of stem cell treatments).

The translation of innovation in the fields of science and medicine into therapeutic products - also known as translational medicine - has revolutionised the way scientists view modern medicine and health care in general. Despite opposition, the Vatican ventured into the stem cell arena, attempting to address preconceived misperceptions about their support for regenerative therapies. By backing NeoStem, the Vatican showed their support for regenerative therapies using ASCs as alternative to ESCs. To their credit, they have realised that in our modern society, the church cannot afford to stagnate or to be indecisive. Modern-day believers are increasingly confronted with how to marry their belief with scientific progress. This dilemma becomes more difficult when religious beliefs are contrasted with developments aimed at alleviating human suffering. The church thus needs to provide a solid foundation for dealing with contemporary issues.

Despite the obvious marketing benefits to NeoStem, it is the authors' opinion that the company used the Vatican as the 'moral microphone' through which to market their ASC therapies to the religious masses. They hoped to reach people who have been confused by ethical concerns and debates surrounding ESCs and who as a consequence have avoided the stem cell arena altogether. NeoStem appears to have wanted to raise public support for the use of ASCs by pacifying concerns related primarily to ESCs and by placing the Vatican's "religious stamp of approval" on their progress, as articulated by their chairman Dr. Robin Smith: "It's like when you have the Good Housekeeping seal of approval, this is the Vatican seal of approval."

Even though their motives were probably less altruistic than claimed, there is a lot to learn from the Vatican-NeoStem interaction. The conference and the ideas that emanated therefrom emphasize the need for a holistic approach to science and scientists' roles in the community and the world. Philosophical questions regarding human existence and suffering continue to challenge our implied and expected ethical and moral responsibility, requiring scrutiny and dissection of own motives, agendas, values and beliefs.

Can science and religion truly find common ground as partners in a mutual effort to find cures to alleviate the suffering of many? The Vatican believes they can, on condition that life is sustained and improved without compromising social and scientific integrity and clearly defined ethical and moral principles.

The unique South African mix of diverse cultures and religious practices and beliefs adds a further degree of complexity to the situation and necessitates a solution to the science vs. religion debate. Inefficiency to bring about effective scientific translation to the public could potentially have a deleterious impact on the efficacy of implementing (novel) medico-scientific discoveries in the South African context. It is therefore imperative for South Africans to find a solution to educate the public with regards to medico-scientific progress while being sensitive to cultural and religious practices.

The author believes that science and religion should complement and strengthen each other and that interdisciplinary collaborations are required to bring a holistic view to an increasingly interconnected world. However, for someone with a different world view, this might not hold true and in that regard, compromise can only extend so far... Certain core values and beliefs are irreconcilable because those values often define an entity, and compromise of those values will necessitate a change in identity, giving rise to a loss of character, which few are willing to accept.

Subsequently it was important to establish the extent of cultural and religious influences on public support for the establishment of an umbilical cord blood stem cell bank in South Africa.

# CHAPTER 4

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## **4 Pilot social response study for the establishment of a public human umbilical cord blood stem cell bank in a selected South African population**

### **4.1 Introduction**

There is a large unmet need in South Africa for bone marrow transplantation. Since its establishment in 1991, the South African Bone Marrow Registry (SABMR) has registered circa 70 000 potential donors. More than 70% of these individuals are Caucasian and are hence not representative of South African demographics (BMDW, 2011). Most of the samples available in the SABMR are thus not genetically compatible with the majority of South Africans and precludes them from benefiting from the SABMR.

The SABMR, as with bone marrow registries across the world, has as a further drawback, namely a donor attrition rate of about 25% (Crookes et al., 2007). This greatly hampers efforts that go into finding an adequate match with further time and cost implications. For this reason umbilical cord blood (UCB) is seen as a viable alternative source to bone marrow (BM) (BM itself or mobilized peripheral blood stem cells (PBSCs)) for bone marrow transplantation.

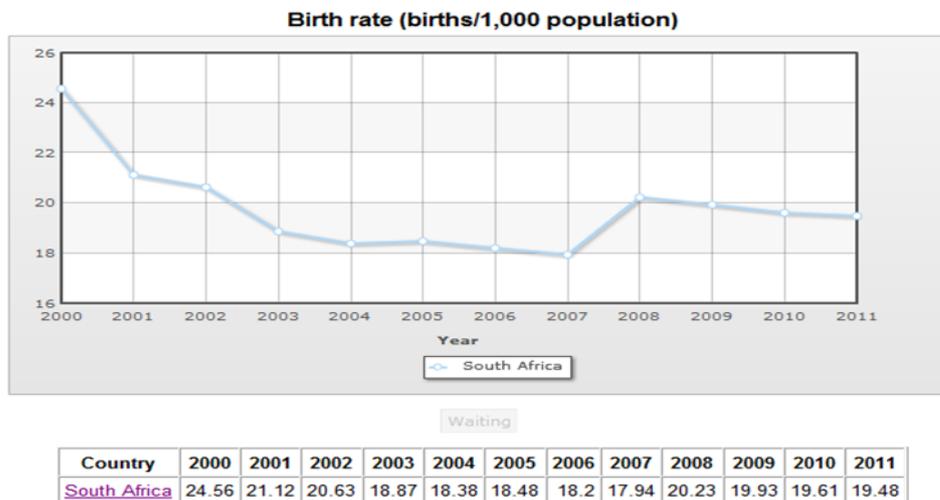
Haematopoietic stem cell transplantation is indicated for the treatment of various conditions including malignant and non-malignant haematological disorders, immune deficiencies and certain genetic disorders. UCB is an important source of haematopoietic stem cells (HSCs). Haematopoiesis, the formation of blood cells, is achieved by lineage-specific differentiation of haematopoietic stem cells (HSCs). HSCs are undifferentiated precursors of myeloid and lymphoid cells, mainly residing in adult bone marrow but can also be found in peripheral and umbilical cord blood.

HSCs are characterized by multipotency and the ability to self-renew. They are known to home to sites of injury and have the capacity to reconstitute the entire haematopoietic system post ablation (irradiation or myeloablation) ) (Kavanagh and Kalia., 2011; Lewis, 2008; Shizuru et al., 2005). Furthermore, UCB HSCs display a greater tolerance toward HLA-mismatch than stem cells from bone marrow or peripheral blood which increases the chances of finding an adequate match for transplantation. With cord blood a minimum requirement of a 4/6 match HLA-A, -B, -DRB1 maternal and paternal alleles is needed while BM and PB require a 9-10/10 match of HLA-

A, -B, -C, -DRB1 and -DQB1 maternal and paternal alleles (Wagner et al., 1996; Hough et al., 2009).

According to Brunstein (2007), multiple studies have demonstrated the efficacy of cryopreserved UCB stem cells from 4-6/6 HLA-A,B antigen and DRB1 allele matched unrelated donors. These studies were done in patients with haematological malignancies and the UCB units were found to contain sufficient numbers of HSCs to engraft most paediatric patients (Brunstein et al., 2007; Gluckman and Rocha, 2006).

In South Africa, blood found in the umbilical cord and placenta is routinely discarded post-delivery. With around 20 births per 1000 individuals in South Africa (Figure 2), we theoretically have an abundant and regular supply of UCB units that are likely to be genetically compatible to the majority of South Africans (Anon, 2009). Furthermore, the umbilical cord itself contains large numbers of mesenchymal stem cells (MSCs), in what is known as the umbilical cord's 'Wharton's jelly'. Mesenchymal stem cells are known to have immune-suppressive properties and co-transplantation of these cells with HSCs could contribute to successful transplantation with decreased risks of GvHD.



**Figure 2: Annual birth rates from 2000 to 2011. This crude birth rate indicates the number of live births per 1,000 mid-year South African population. (Used with permission from The World Factbook (Anon, 2009)).**

Collecting UCB is a non-invasive procedure and once collected, the purified stem cells can be stored indefinitely until a unit is needed. Storing these units in stem cell banks (SCBs) throughout South Africa, could thus serve as a vital, easily obtainable resource.

It is still unclear how much cell viability is affected over longer periods of cryopreservation (>25 years). However, promising new techniques in UCB expansion and innovative uses for UCB - such as the generation of induced pluripotent stem cells (iPSCs) - potentially increases the value and need for stored UCB units for the future (Broxmeyer, 2010; Gilmore et al., 2000; Kedong et al., 2010). iPSCs are differentiated somatic cells that have been de-differentiated through genetic engineering, to revert back to their embryonic-like state. These cells are thus pluripotent, have the ability to migrate and self-renew. They could be coaxed into differentiating into several cell lineages and has enormous potential for future autologous use.

Together with a greater tolerance for HLA mismatches, the use of UCB for bone marrow transplantation results in a lower incidence of graft vs. host disease (GvHD). There are no ethical concerns for using UCB as source of stem cells as opposed to those encountered with embryonic stem cell research and no risk of donor attrition (Hough et al., 2009). This makes UCB a safe, convenient and reliable resource of stem cells (Crookes et al., 2007; Rogers and Casper, 2004).

Many South Africans are currently unable to access these treatments due to a lack of HLA-matched bone marrow (BM) or UCB units and would therefore benefit directly from UCB units stored in a public bank. Establishing an UCB bank would assist the government to give effect to the right of each person to access to health care services. The state is obliged to progressively realise this right as stated in section 27(1)(a) and 27(1)(b) of the Constitution of the Republic of South Africa, 1996.

However, South Africa has an extremely high prevalence of Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome (HIV/AIDS). In mid-2007, following the latest antenatal survey, the Department of Health, in collaboration with UNAIDS, WHO and other groups, published an updated estimate for HIV prevalence of 18.34% in people aged 15-49 years old in 2006. This equates to around 5.41 million people living with HIV in 2006, including 257,000 children. The ASSA2003 model provides a similar estimate of 5.4 million people living with HIV in mid-2006, or around 11% of the total population. It predicts that the number will exceed 6 million by 2015, by which time around 5.4 million South Africans will have died of AIDS (UNAIDS, 2010). .

Statistics from 2011 show a slight decrease, estimated at 10.6%, in overall HIV prevalence since 2006. The total number of infected individuals is estimated to be 5.38 million with 16.6% of adults aged 15-49 years being infected. The total number of new infections was estimated to be 316 900 of which 63 600 were children below the age of 14 (UNAIDS, 2010). Consequently, all UCB units considered for banking, will need to undergo rigorous testing and screening, prior to acceptance for storage.

The sensitive Ultrio-Plus® assay is currently performed on all blood donations received at the South African National Blood Service (SANBS) and is internationally accepted and highly successful (Crookes et al., 2007), but has not previously been verified for screening of UCB.

## 4.2 Materials and Methods

The process of informed consent is often reduced to only obtaining consent without truly informing the patient of benefits, risks and alternatives and ensuring that the patient understands the information. However, investigators have a moral and ethical duty not only to obtain consent, but also to ascertain that all components of informed consent are satisfied, i.e., disclosure, understanding and appreciation, capacity and voluntariness. The challenge of obtaining informed consent was particularly demanding due to our unique South African context.

The objective of the social response pilot study was to gauge public reaction towards and support for UCB stem cell donation and banking, as well as their perception of the processes of donation and subsequent HIV testing of UCB (necessary for compliance with international regulatory standards). A concise interview and questionnaire were constructed to convey information about the study. Balancing simplicity with accuracy and comprehensiveness was essential in order to make the information accessible to everybody and simultaneously address related questions and concerns. The anonymous questionnaire – in the structure of an informed consent document – was completed by the target population: mothers attending the ante-natal clinic in the Steve Biko Academic Hospital in Pretoria and consisted of three questions:

**Question 1:** Would you be willing to donate your placenta (afterbirth) to medical research?

**Question 2:** Would you be willing to undergo an additional HIV test seven days before or after the birth of your baby?

**Question 3:** If it is against your cultural or religious belief to donate your placenta for medical research, would you be willing to donate the blood from the placenta?

77 mothers were randomly selected to partake in the pilot study. Signed informed consent was obtained after they completed the closed questionnaire.

Visual aids (a doll with an umbilical cord and placenta and relevant posters) were used to explain concepts relating to UCB banking during the interview. Questions that arose from the interview were annotated by the investigators and used to reconstruct the interview process and questionnaire for the principal study. The quantitative data gathered from the

questionnaires was captured and analysed using Microsoft Excel while qualitative data was gleaned from patient comments written on the questionnaire.

Approval for this study was obtained from the Main Research Ethics Committee at the University of Pretoria (131/10) and subsequent amendments that were deemed necessary were submitted and approved by the same committee. Ethical approval was valid for the duration of the study (2010 – 2012) and the final approval document is attached as Annexure 5.

## **4.3 Results**

### **4.3.1 Qualitative results**

#### **4.3.1.1 Introduction**

With these principles in mind, the investigators addressed the mothers attending the ante-natal clinic at the Steve Biko Academic hospital in Pretoria. Their responsibility was to introduce the mothers to stem cells in an easily accessible manner while maintaining a realistic scientific view of the field. Although conflicting views and opinions regarding current, acceptable stem cell treatments exist, it was important for the investigators to convey a balanced, realistic view of current and future possibilities with stem cell treatments. Imparting understanding to the patients equipped them to make informed decisions. The patients' contribution to the study was clarified at the onset of the interview, giving them the freedom to choose to participate or not.

The investigators encountered various obstacles which eventually shaped the structure of the principal study. These obstacles are discussed as qualitative results from the interview process and include; ill prepared clinical settings for obtaining informed consent, cultural differences, religious practices, traditions and superstitions together with language constraints and educational disparity. Clarification regarding cell harvesting, storing and administration was compulsory together with an explanation of existing and possible future applications of stem cell treatment.

#### **4.3.1.2 Patient interaction**

It was vital to establish and maintain good inter-personal relationships with hospital staff and attending mothers to ensure a good and effective working relationship. People interaction is dynamic and required a perceptive and creative investigator to ensure active and continued

patient involvement. A relaxed and spontaneous environment facilitated a trust-relationship and patient participation. Given South Africa's history of Apartheid, dispelling fears and enkindling trust in a country wrought with racial conflict and mistrust is no small feat to accomplish.

Physical and logistical distractions provided by the environment in which the interviews were conducted complicated the interview process. The interview had to proceed concomitantly with routine administrative procedures taking place within the waiting room. Attending patients were constantly distracted by staff during the interview for administrative purposes related to patient files and by being sent away for blood tests, urine tests and patient weight). Furthermore, no time-slots were allocated to arriving patients who were treated on a first-come-first-serve basis, which contributed to the disarray. These circumstances effectively limited the interview to an interrupted 15 min. contact period.

Questionnaires were only handed out after the interview so as not to serve as an additional distraction. Asking general questions that served as leads to the next explanation in the presentation was very successful with regard to involving the patients. Upon first introduction to the study, some patients were reluctant to fill out the questionnaire and requested to discuss the information with family or friends. However, patients visit the clinic frequently and some returned with questions, while others filled out the form on a second or third exposure to the study.

This could have been due to patients becoming better acquainted with the study, the investigator and concepts which improved participation and dismissed initial prejudices. Initial concerns might have been addressed on a second exposure while peer pressure could have also coaxed patients into participation.

Given the circumstances, it was most beneficial to address the patients as a group. Patients were less intimidated by foreign concepts by not being isolated from the group; they were exposed to questions raised by others; were able to ask related questions and to interact amongst themselves in their own language in discussions which the investigator facilitated. One-on-one interviews were performed with individuals that did not understand English. One-on-one interviews were unfortunately not always possible, given time constraints, inadequate space and the lack of an interpreter.

The above-mentioned constraints necessitated a concise interview and informed consent questionnaire. The use of visual aids (in the form of posters and a doll with umbilical cord and placenta) greatly contributed to the clarity of the information presented and improved patient interaction. It held patients' attention and clarified foreign or difficult concepts concerning UCB collection and banking. The waiting room was unfortunately not equipped to use projectors or video, valuable tools to convey information – which could be especially beneficial in the absence of a translator.

#### **4.3.1.3 The language barrier**

English was used to convey the information during the informed consent presentation. South Africa has 11 official languages and many South Africans speak English only as a third or fourth language. Many patients' understanding was thus limited to that of basic conversational English. This understanding was often insufficient for them to grasp more technical concepts concerning stem cell banking and was arguably the biggest stumbling block in obtaining consent.

A succinct presentation, clear and to the point, with comprehensible English terms and short sentences, helped to make the presentation more accessible to non-English speaking patients. Concepts such as “placenta”, “stem cells” and “public SCB or facility” remained foreign. These concepts were better explained through analogies or translating the words into other languages e.g. “placenta” translates to “ingubo” in Zulu and “gobo” in Tswana and means “blanket”. It is commonly understood to “cover the baby in the womb”.

There was limited access to a translator at the onset of the pilot study. After identifying a need for translation, a colleague joined the investigators during the presentations to assist in translation of the presentation, or parts of the presentation, into Zulu and Tswana.

Having a translator present was beneficial even to the patients that understood most of the presentation in English. It gave some patients more confidence to clarify concepts and ask questions in their own language. It particularly helped when patients with no understanding of English came to visit the clinic and the translator often conducted one-on-one interviews with these patients. Translation of the informed consent questionnaire into some of the commonly spoken languages will ease the strain of communication and clarification of concepts.

#### **4.3.1.4 Culture and Religion**

Culture and religion are often closely associated and certain cultural aspects or religious practices had to be taken into consideration during the interview. Together with cultural practices from South African citizens, the investigator encountered cultural practices in immigrants from neighbouring countries. Some of the countries that were represented included Somalia, Zimbabwe, Angola and the Congo.

#### **4.3.1.5 Cultural practices**

The pilot study's questionnaire unfortunately did not make provision for recording patient ethnicity. For the purpose of building public SCB facilities in different provinces, it would have been beneficial to segregate the data into cultural or religious groups. This segregation in turn could aid in the identification of customs potentially conflicting with the requirements for establishing a SCB. Knowing whether certain practices are more likely connected to a specific language or cultural group from a certain geographical area would have aided in choosing locations for cord blood collection. These changes were incorporated for the compilation of the principal study's informed consent questionnaire.

Given South Africa's diverse cultural and religious background, it becomes imperative for investigators to at least understand the fundamentals of cultures and religions when addressing the patients, in order to anticipate sensitive topics or misconceptions and address them appropriately.

#### **4.3.1.6 Social rules of engagement**

As mentioned previously, all mothers attending the ante-natal clinic at the Steve Biko Academic Hospital were addressed during an interview. At the onset of the study, patient interaction was limited. Some of the older women (between the ages of 30-50) seemed to be more hostile towards the investigators. Although the study did not set out to test the influence of pre-existing prejudice, this could be due to such prejudices regarding people from different races, a sad memento from our past, or could be ascribed to differences in "social conduct". Even though our country bears the scars of Apartheid, most women addressed at the clinic seemed to nevertheless have moved past the prejudices of race.

The investigators probed patients about their reluctance to participate and reasons given related to topics of "social conduct" and "social hierarchy". Certain cultures regard elderly

people as having a higher social status, which demands more respect than peers it is also regarded as disrespectful for a younger person i.e. the interviewer, to ask an older female about childbirth beliefs and practices. A young person would not be allowed to ask questions or speak out when an older person is present, regardless of the younger person's knowledge concerning the topic. It is seen as disrespectful and would be frowned upon by members of that community. Similarly, when a speaker addresses a group – such as the investigator - that speaker is seen as learned, wise or knowledgeable. Only certain elders would be allowed to address that person directly or ask him/her questions. Questions should thus be kept to oneself or should be directed at others present after the presentation, for fear of insulting the speaker or the elders present.

The investigators were unfamiliar with these concepts and fears as would be most people who are not of African origin. Patients' fear and hesitation translated into unasked and unanswered questions contributing to a lack of understanding of the concepts involved with UCB banking. Consequently patient feedback was lacking and many questionnaires were left unanswered.

By addressing these concerns, encouraging patients to ask questions (even if only amongst themselves) and leading them with questions, the investigators were able to overcome these cultural hindrances. By facilitating a discussion amongst the attending mothers, many more mothers were involved and supportive of the study.

When questions were asked, they served as valuable tools to structure the presentation and questionnaire, to eradicate all ambiguities and clarify concepts in the interview. Without this necessary feedback, it was difficult to gauge the patients' level of understanding.

#### **4.3.1.7 Religious ritual practices**

Certain ritual practices related to the placenta were also encountered. Instead of discarding the placenta in the normal way (incineration at the hospital), some religions retain the placenta after birth for various reasons. Reasons range from rituals of burying the placenta to eating it. These patients were not willing to donate their baby's placenta and umbilical cord to medical research or in some cases for the blood to be collected from the placenta after birth.

Together with some of these ritual practices, there are many superstitions and beliefs, often accompanied by fear. Some groups believe that blood constitutes a "special life power". Should anybody thus take blood from e.g. the placenta, they will take the "life power" from the

child and put this child at a disadvantage. Other patients expressed concerns in seeing the placenta, since they believe this will put a curse on the child's life with deleterious consequences for the child's future.

#### **4.3.1.8 The influence of traditional medicine**

Many Black South Africans strongly adhere to traditional medicine in various forms, some more accepted than others. Some mothers-to-be were afraid that blood samples (or the placenta) would be used for "muti" – a controversial form of traditional medicine. The stigma surrounding "muti" comes from occasional "muti-murders" where mostly very young or very old people are either murdered or mutilated in order to obtain organs or body parts for use as ingredients in "muti-medicines". When the investigator unwittingly talks in layman's terms of how stem cells can be used as a type of a "medicine" to "cure" certain diseases, he/she could immediately raise concerns about "muti" if this is not clarified and taken into consideration by the investigator during the interview.

#### **4.3.1.9 Stigma surrounding HIV status**

HIV/AIDS education has come a long way in South Africa but a lot more still needs to be done to address social prejudices and fears. This is particularly true when considering the very high HIV prevalence in our country and the continuing stigma and mysticism that surrounds HIV/AIDS.

Patients were often afraid that their HIV status would be revealed during or as a result of the interview process. Some were afraid of being victimised, of not receiving proper treatment or of being treated with contempt or disdain. Some mothers were reluctant to take HIV tests for fear of knowing their status while some were afraid of needles and the drawing of blood. One patient admitted to the investigator to being HIV infected and was reluctant to donate blood in fear of accidentally infecting another person with HIV.

Since all UCB samples need to be screened routinely for infectious diseases, including HIV, in order to be accepted nationally and internationally, a patient's refusal to do an additional HIV test at the time of delivery of the child would lead to the non-inclusion of that sample into the storage facility.

#### **4.3.1.10 Educational disparities**

As a general rule, the interview and questionnaire were structured to be easily accessible and understandable. Some patients were unable to read while others could not read in English and

were mostly reliant on understanding the information from the presentation. Some of the attending mothers had not completed their schooling, not uncommon in South Africa, and consequently lacked foundational understanding about English and often biology.

Questions that arose from the presentation can be divided into three main categories: Questions concerning female biological processes, questions related directly to the presentation and medically related questions.

#### **4.3.1.11 Biologically related questions**

Some patients lacked a general understanding of normal female health and reproduction. This led to questions relating to the origins of the placenta, menstruation, the role of the placenta during and after pregnancy. A few patients had concerns primarily centred around the placenta: how many children they could have after donating a placenta; whether a person can live without a placenta; how many placentas a mother expecting twins has; and whether the placenta could be donated after a miscarriage.

#### **4.3.1.12 Questions directly related to the study**

Patients were initially unsure of the blood collection procedure. Before introducing visual aids to support the presentation, some patients confused donating the blood from the placenta with organ donation. Some patients were afraid of, while others were excited at, the prospect that they could allegedly be sterile after donating the placenta or blood from the placenta.

Other questions included the volume of blood to be collected, where and from whom the blood would be collected, and the subsequent storage and redistribution of the collected blood. Some did not understand the necessity for additional HIV tests on patients that have already undergone HIV tests.

Additional questions regarding the technical side of UCB banking had to be addressed, complicating the interview process: Mothers had to understand the current uses of UCB, together with the prevalence of disorders that could be treated with a BMT using UCB. They often enquired about an individual's eligibility for a transplant and the subsequent procedure of obtaining an appropriate UCB unit. Some mothers were concerned about the availability of a sample and about finding an appropriate match should they require it.

#### **4.3.1.13 Medically related questions**

These included questions related to congenital disorders, alcohol abuse, the subsequent eligibility of that person to donate their UCB and situations relating to twins.

Some of the above mentioned questions could have been easily addressed by rewriting the interview and clarifying concepts during the presentation. However, as the investigators were not qualified medical physicians, these questions were referred to the doctors on duty. Learning which questions to answer or refer to medical doctors required sensitivity to each situation and added to personal development of the interviewers. Processes of Banking

The notions of stem cells and banking were foreign to most of the attending mothers and they therefore needed to be assured of the stem cell banking technology, its efficacy and applications. The processes involved in UCB banking - from harvesting the UCB immediately after delivery, to sample processing, storage and redistribution - had to be explained thoroughly. This was particularly important given the fears of organ trafficking and the use of body parts in certain traditional medicine cocktails referred to earlier (“muti”). Furthermore, it was necessary to provide a clear motivation for the study and how South Africa could benefit from having a public SCB. The benefits of having a public and/or private bank had to be addressed without partiality – a contentious topic requiring unbiased diplomacy.

Based purely on our circumstances in South Africa, there is a strong motivation for establishing a public SCB. One of the strongest motivators is the great genetic diversity in our population and the consequent lack of compatible sources of bone marrow or UCB to treat the majority of South Africans. The people’s need for access to healthcare and specialised treatment outweighs most arguments against the establishment of a public SCB in South Africa, with the exception perhaps of financial considerations. This would respond to the ethical imperative of access and equity, and hence social and distributive justice in the country.

#### **4.3.1.14 Personal obstacles**

Learning how to build a patient-interviewee trust relationship was vital to ensure successful interactions with the patients. Learning what to say, how to say it and when and how to refer difficult questions, was one of the fundamental hurdles that needed to be overcome in order to successfully complete the interview.

Due to the novelty of the particular study, it lacked appropriate protocols and format for addressing the patients. Information conveyed was too broad, lacking direct relevance to the study. Instead of informing patients, details given regarding rituals and practices fed existent concerns and uncertainty amongst the patients. It gave way to a fear of unknowingly becoming involved in cultural or religious taboos. As a consequence, patients were reluctant to fill out the questionnaire and wanted to consult with their elders regarding their cultural practices before becoming involved in the study.

All irrelevant information confused the patients and detracted from information that was important. Questions from the mothers-to-be helped to point out discrepancies and uncertainties that arose as a direct consequence of the lack of experience or training of the interviewers. Feedback from patients was encouraged at all times and used as positive criticism to improve the questionnaire and interview process.

The nature of the interview/presentation and difficult questions (because of moral, ethical or legal reasons) that arose in these areas prompted a revision of the questionnaire, presentation and interview process. All changes were incorporated into a principal social response study (discussed in Chapter 5).

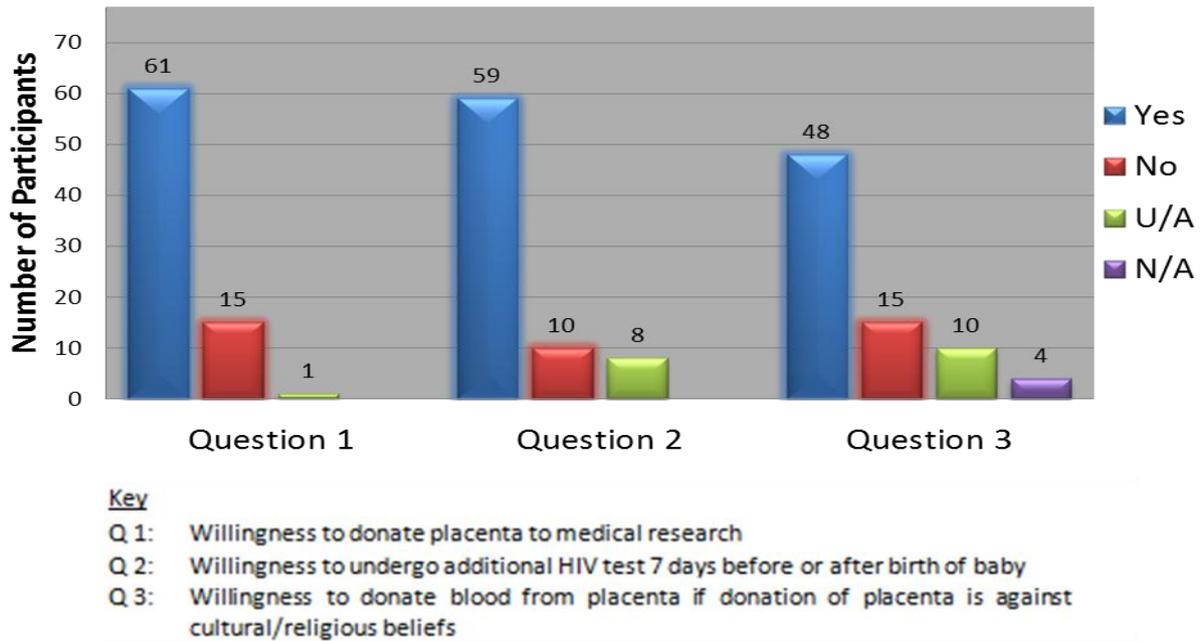
### **4.3.2 Quantitative results**

#### **4.3.2.1 Introduction**

Although a few routine medical procedures exist that involve UCB transplantation, there are many more possibilities for potential treatments that could be explored. With vastly improving techniques for expanding haematopoietic stem cells (HSC) in culture, it is possible that samples stored in public banks will become a vital resource for novel forms of therapy in the future. It was therefore deemed beneficial to include in the questionnaire the possibility that samples could be used for medical research and/or public use. The term “medical research” was used to describe all downstream applications that involve current and possible future treatments with UCB. A clear distinction was made during the interview process between the current use of UCB for transplantation and research purposes.

#### 4.3.2.2 Results

Results from the social response pilot study questionnaire are summarised in Figure 3.



**Figure 3: Summary of results from the informed consent questionnaire. Numbers above the bars in the graph indicate the number of patients that answered the particular question, out of a total of 77. Answers with either “Yes” – indicated by blue bar, “No” – red.**

The patient cohort in this pilot study was intentionally small (77 patients) and was limited to patients attending the ante-natal clinic at Steve Biko Academic Hospital. Many of the mothers-to-be attending this clinic are high risk pregnancies and are often referred by their local clinics. It can be argued that these mothers receive more information regarding their pregnancies and might be more educated and have better access to information concerning their pregnancies than mothers attending other clinics. This could have facilitated the presentation of information to the mothers at this clinic, and it was understood that it might be more difficult to convey the same information in rural clinics.

As previously mentioned, initial participation in the study was poor. Many more patients filled out the questionnaire after adjusting the interview process to eliminate some of the uncertainties and fears discussed. Data gathered from the questionnaire seemed to indicate that administrative procedures, interview language and a person’s education played the biggest roles in determining participation in the study. Cultural and religious concerns and HIV status only accounted for 7% of expressed reluctance towards establishing a SCB. These results need

to be confirmed however, in a larger study with different patient demographics in order to obtain statistical significance.

Despite the interviewer's efforts, some questions in the questionnaire were sometimes left unanswered (U/A) (Figure 3). This could either be an indication that the patients did not understand the question, were undecided or reluctant to answer (e.g. to undergo an additional HIV test) or were not able to complete the questionnaire because of time constraints (e.g. called by a nurse or doctor).

Of the 77 participants, only 51% (40 participants) answered "yes" to all three questions. 79% of the patients (61 patients) answered "yes" to Question 1, indicating a willingness to donate their placenta. Seventy six percent of the patients (59 patients) were willing to undergo an additional HIV test (Question 2) and 62% (48 patients) were willing to donate the blood from the placenta to medical research (Question 3) (Figure 3).

There was a discrepancy found between Question 1 and 3 in 8% of the questionnaires: 12 participants that were willing to donate the placenta itself, were unwilling to donate the blood from their placenta (Question 3).

It might be argued that 8% of the participants answered "no" to the first part of Question 3 "If it is against your religious or cultural belief..." indicating that it is not against their cultural belief and that they would donate the blood from the placenta. However, it could also indicate that they did not understand that by donating the placenta, they were giving permission to use the blood from the placenta, thus contradicting their answer in Question 1.

Only 3 patients (4%) had a problem with donating their placenta, but all 3 were willing to donate the blood from the placenta. This could be an indication that cultural or religious practices might play a much smaller role in obtaining informed consent than initially anticipated. It cannot be ruled out though that people living in the city possibly adhere less to their cultural practices than people of the same culture that live in rural communities due to different exposures and influences from other cultures. The ages of the patients completing the questionnaires were also unknown. Younger people could be more willing to fill out the questionnaire and might be more liberal concerning cultural practices and traditions.

Patients seemed less intimidated by undertaking an additional HIV test. Of all the patients that were willing to either donate their placenta (Question 1; 79%) or the blood from their placenta (Question 3; 62%), only two patients (3%) were unwilling to undergo an additional HIV test (Question 2). This could be due to the fact that all of the attending patients at the clinic had previously undergone an HIV test and their HIV status was known to them. The issue of a possible change in HIV status after testing in early pregnancy was not addressed. Mothers that attend a rural clinic for the first time might however not know their status and additional fears regarding HIV status and testing might be an obstacle to deal with in the principal study.

Not all of the cultural groups in South Africa were adequately represented and results obtained from the pilot study can thus not be extrapolated to the whole of South Africa. Similar studies will need to be conducted in different provinces and in clinics, private and public hospitals, in order to obtain a clearer picture of the influence of demographics, cultural background and socio-economic status across South Africa with regard to social acceptance and response of UCB banking.

#### 4.4 Conclusion

Obtaining informed consent is an intricate process. In our efforts to address mothers at the Steve Biko Academic hospital, a few hurdles needed to be addressed prior to considering the question of establishing a public UCB SCB.

During the first few months various difficult situations and potential problems were encountered. Mothers were initially unreceptive and reluctant to fill in the questionnaire. Administrative, time and physical constraints impeded the efficacy of the interview process. Because there were many uncontrolled distractions, the investigators had to take heed not to add more distractions to the interview themselves with an incoherent presentation. The investigators had to address patients and situations with care and sensitivity toward opinions and perspectives. These initial difficulties were leveraged to construct a better organised and more coherent interview process as the pilot study evolved.

Certain aspects of the interview process can in future be facilitated by improving infrastructure at the clinic and by creating a specific uninterrupted time-slot to obtain consent, while others could be addressed through educating the general public on these matters.

During the interview, the subsequent inclusion of visual aids contributed to facilitating the explanation of concepts inherent to stem cell banking. It promoted the mothers' involvement by providing a platform for accessibility to the new technology and gave an opportunity to ask questions. This helped to visualise components of what was to many, a new and strange concept, thereby helping to minimise fears and superstition. In addition, translating key concepts or words - such as "placenta" - into different languages enabled a more coherent understanding of the process of UCB collection prior to banking. The questionnaire was expanded to include six questions related to UCB SC banking as well as personal information about the patient (Annexures 1 and 2). Results for the revised questionnaire are discussed in Chapter 5.

Preliminary results shed light on cultural and religious practices and linguistic and academic insufficiencies that could influence community support for a public SCB. Gathering information on the ethnicity of these patients would thus be imperative.

Some inconsistencies in answering the questionnaire indicated a need for better structured questions and improved clarity in the interview. These inconsistencies highlighted areas of confusion and shortcomings in the interview process as well as the questionnaire layout which necessitated amendments to both the interview outline and the questionnaire. A revision of our methods in conveying the purpose and utility of a public SCB helped to overcome fears and public misconceptions and contributed to educating the public as to their role in public banking.

Educating the general public with regard to the workings and benefits of public SCB is the first step to determine the viability of such an undertaking – a unique and rich challenge in our South African context. Education will have the greatest impact if children or young adults could be educated about stem cells, the future of stem cell treatments and UCB banking through integrating the work into the school curriculum.

In our South African context, we are faced with unique and rich challenges relating to cultural and religious differences that are further enriched by linguistic constraints, educational insufficiencies and logistical and administrative limitations. However, none of these provide an insurmountable challenge, and despite cultural or religious constraints, the majority of the general public that we interviewed are positive about establishing a public UCB SCB for South Africa. The results are however not definitive and need to be verified in different demographic and socioeconomic settings across South Africa. It is thus up to the team of investigators to find innovative solutions to the few remaining obstacles and to verify the initial positive results through a more extensive and definitive social response study.

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