Summary and Conclusion

Stem cells hold great promise for regenerative medicine because of their ability to self-renew and to differentiate into various cell types depending on the stimuli (signals) that they received. Stem cells are classified into embryonic stem cells (ESC) and adult stem cells (ASC). Whereas ESCs are derived from the inner cell mass of a blastocyst, ASC usually originate from various tissues of a developed individual (adult) and they are alternatively called somatic stem cells.

The potential differentiation of stem cells is classified into totipotent, pluripotent and multipotent. A fertilized egg is totipotent and can differentiate into any cell type. An ESC is pluripotent and can differentiate into any cell type, except a fertilized egg. An ASC is multipotent and can differentiate into most cell types of its tissue origin

However, numerous studies have shown that ASC can differentiate into cell types beyond their tissue origin (e.g. bone marrow stem cells [BMSC] differentiating into cardiomyocytes); therefore, ASC appear to possess a certain degree of pluripotency. In any case, although ESC is undoubtedly superior to ASC in differentiation potential, its research has been restricted by ethical concerns and governmental restrictions. ASC research, in contrast, is moving faster and has reached clinical trials ahead of ESC research.

Various types of ASC have been discovered in various tissues, the largest class being the mesenchymal stem cells (MSC), which reside in virtually all post-natal organs and tissues. Among various types of MSC, are the BMSC and hematopoietic stem cells (HSC) which were discovered the earliest and have been investigated most thoroughly.

Available evidence points to the role of BMSC as replacement cells for the routine maintenance of normal tissues, such as in the kidney, and for the repair of damaged tissues, such as in an infracted heart. Hundreds of reports have collectively shown that BMSC can differentiate into various cell types including adipocytes, endothelial cells, epithelial cells, glial cells, hepatocytes, neurons, cardiac muscle cells, skeletal muscle cells and smooth muscle cells. Furthermore, many of these reports have used animal models to demonstrate the feasibility of using BMSC for treatment of degenerative and inflammatory diseases.

More recently discovered adipose tissue-derived stem cells (ADSC) are virtually identical to bone marrow stem cells (BMSC) in differentiation and therapeutic potential, but are easier, safer to obtain and can be harvested in larger quantities. Therefore, ADSC appear to be a better choice for future clinical applications. ADSC could restore the erectile function of neurogenic ED which frequently occurs to patients who have undergone pelvic floor surgeries or radiation.

This study aims to research the application of *stem cells* in andrology and their role in treating erectile dysfunction and male infertility. Compared with other fields, Andrology has been relatively late to embrace *stem cells* as potential therapeutic agents, with researches being concentrated in two areas: Erectile dysfunction (ED) and male infertility. Ten to fifteen percent of couples are infertile. Approximately 50% of human infertility is attributable to male defects with the clinical presentation of abnormal sperm production, such as oligo-, atheno-, teratospermia or azoospermia. At present, treatments for male infertility are limited and, most often, a range of in vitro fertilization (IVF)

techniques are used to circumvent rather than treat male infertility problems. Intracytoplasmic sperm injection (ICSI) is most frequently used in cases of male infertility. The development of ICSI has made it possible to use individual sperm or germ cells recovered from various maturation stages for fertilization.

In regard to male infertility, in this study it was showed that ESC could form male germ cells *in vitro*. Specifically, they showed that the differentiation of ESC into male germ cells depend on embryoid body formation and was greatly enhanced by the inductive effects of bone morphogenic protein 4-producing cells. It was further showed that the induced germ cells could participate in spermatogenesis when transplanted into reconstituted testicular tubules, demonstrating that ESC can produce functional germ cells *in vitro*. It was also shown that human stem cells can develop into the earliest stages of sperm cells but have gone no further than that because of ethical concerns and many safety aspects that must be fist resolved and this could take years.

"Who is the father of offspring born from laboratory sperm- a collection of stem cells in a Petri dish? The embryo from which these cells were derived? The answers to these questions are not clear but they go to the foundation of our sense of identity."

Another landmark was reached when it was shown for the first time that human BMSC could differentiate into putative human male germ cells. It was also shown that BMSC transplanted into the testis of an infertile mouse model appeared to differentiate into germ cells, Sertoli cells and Leydig cells. This finding raised the possibility of using BMSC to treat male infertility and testosterone deficiency.

In regard to erectile dysfunction, BMSC transduced with eNOS were able to improve the erectile function of aged rats. Also ESC

transfected with brain-derived neurotrophic factor (BDNF) could restore the erectile function of rats whose cavernous nerves were experimentally damaged. BMSC alone or transduced with eNOS were able to reverse age-associated ED. Human BMSC transplanted into rat corpus cavernosum was able to differentiate into endothelial and smooth muscle cells. And finally the ADSC that can restore erectile function in neurogenic ED. Although the number of patients who have been treated with ADSC is still too small to make ADSC the obvious choice among the various types of stem cells, one additional factor to be considered is that ADSC has been used commercially to treat more than 2500 horses with an approximate success rate of 75%. Therefore, the evidence for ADSC as a regenerative medicine is solid, and it was clearly shown that ADSC is a promising therapeutic entity for treating andrological diseases. The ability of stem cells to produce factors capable of treating carcinogenic cells was also used to treat other andrological problems such as cancer prostate.