
# STEM CELLS TRANSPLANTATION IN MANAGEMENT OF END STAGE LIVER DISEASE

**Essay**

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**General Surgery**

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# زرع الخلايا الجزعية في علاج المراحل المتاخرة من مرض الكبد

رســـالـــــة
مقدمة توطئه للحصول على درجه الماجستير فى
الجراحة العامة

**مقدمة من**

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# INTRODUCTION

While organ transplants have helped victims of liver, they are accompanied by numerous problems. As the demand is far greater than the supply, not enough organs are available for patients in need and patients die while waiting. In addition, after transplants, the body often recognizes new organs as foreign objects, so it may rejects and destroys them. To counter this, patients receive immuno-suppressive medication, rendering their bodies susceptible to bacteria, viruses and cancer. Also they extremely suffer from heavy costs for the remainder of their lives. US Medical Experts say: "Embryonic Stem Cells provide an ideal solution for the problems associated with transplantation. They will allow for almost unlimited organ regeneration". According to US Health Department statistics over 5,000 severely ill patients die each year while awaiting an organ transplant. There simply are not sufficient organs donated to fill the need ***(Asahara et al., 2004).***

Isolation of human stem cells offers the promise of a remarkable array of novel therapeutics. Biologic therapies

derived from such cells, through tissue regeneration and repair as well as through the targeted delivery of genetic material, are expected to be effective in the treatment of a wide range of medical conditions. Efforts to analyze and assess the safety of using human stem cells in the clinical setting are vitally important to this endeavor ***(Fox et al., 1998)***.

The power of stem cells was first harnessed for medical application in 1956, when a pioneering bone marrow transplant was performed by Dr. Donnall Thomas who is, along with Joseph & Murray as co-worker, a winner of the 1990 Nobel prize in physiology and medicine for their discoveries concerning organ and cell transplantation in the treatment of human diseases. Within just a few years, the possibility that the human body contains cells that can repair and regenerate damaged and diseased tissues has gone from an unlikely proposition to a virtual reality ***(Jiang et al., 2002)***.

In 1960 first few cases of successful use of stem cell of bone marrow origin in treatment of congenital immune deficiency disorder and end stage leukemia were reported ***(Brockes et al., 1997).***

Allogenic liver transplantation remains the only effective treatment available to patient with liver failure but Because of serious shortage of liver donors, however, an alternative therapeutic approach is urgently needed ***(Fox et al., 1998)***

Stem cells have two important characters that listing distinguish them from other types of cells. First, they are unspecialized cells that renew themselves for long periods through cell division. The second is that under certain physiologic or experimental conditions, they can be induced to become cells with special functions such as the beating sells of heart muscles or the insulin producing cells of the pancreas. ***(Civin et al, 1984)***

Stem cells are the primordial cells in the human body. The first stem cells occur inside the developing embryo (blastocyst). These embryonic stem cells are understood to be toti-potent (capable of differentiating into every cell type). They divide and differentiate to ultimately construct the entire human body. Stem cells used in regenerative medicine, come from numerous sources, and have demonstrated most surprising ability for

transformation into other tissues and cell types for repair of damaged tissues including liver tissue ***(Wang et al., 2003)***.

Types of Stem cells may be used: ❶ Embryonic Stem Cell (ESC) therapy: involves the use of cells extracted from a 5 day old in vitro fertilized embryo; ❷ Fetal Stem Cell (FSC) therapy: involves the use of human fetus aborted between 1 and 3 months; ❸ Adult Stem Cell (ASC) therapy: involves the use of stem cells derived from the bone marrow;❹ Whole Cord Blood Stem Cell (CBSC) therapy: involved the use of stem cells derived from full term birth; ❺ Purified and potentiated Cord Blood Stem Cell (PP-CBSC) therapy re-involves the use of propriety protocols to remove the white and red blood cells from the cord blood leaving only stem cells***( Asahara et al., 2004).***

Until recently the three major sources of stem cells are bone marrow, peripheral blood and cord blood stem cell. There are two types of bone marrow stem cell whether autologous or allogenic stem cell transplantation ***(Jiang et al., 2002)***.

Human embryonic and adult stem cells each have advantages and disadvantages regarding potential use for cell based regenerative theories. Of course, adult and

embryonic stem cells differ in the number and types of differentiated cells types of they become. Embryonic stem cells can become all cell types of the body because they are pluripotent. Adult stem cells are generally limited to be differentiated into different cell types of their tissue of origin. ***(Gage et al., 1995)***

There are many theories of transdifferntiation which mean conversion of cells from one differentiated type to the other e.g., stem cells can differentiated to hepatocytes . To prove that transdifferentiation was occurred we must prove that the cells acquire the new morphologic and functional and antigenic characters of new organs e.g., transdifferentiation to hepatocytes the new cells acquire large size and acquire new surface antigen (AFP) and appearance of functional product in cell culture which was albumin. Transdifferentiation to occur there is induction stage by nuclear transplantation or manipulation of cell culture condition or uptake of molecules from cellular extract or induction of ectropic gene expression. ***(Wang et al., 2003)***.

Stem cell therapy involves the introduction of healthy new stem cells to repair and replace damaged or

lost cells. This therapy, often referred to regenerative medicine provides much promise for the treatment of what wes previously regarded as incurable diseases. Recently, extra-hepatic sources of hepatocyte lineage cells have been explored in the use for cell therapy. Embryonic stem cells and bone marrow cells have been reported to have the potential to differentiate into multi-lineage cells including hepatocytes,In in-vitro and in-vivo models.***(Chinzei et al., 2002)***

# AIM OF THE WORK

The aim of this work is to focus on stem cell transplantation in cases of hepatic failure.

# DEFINITION AND TYPES OF STEM CELLS

The word stem actually originated from old botanical monographs from the same terminology as the stems of plants, where stem cells were demonstrated in the apical root and shootmeristems that were responsible for the regenerative competence of plants. ***(Brocckes et al., 1997)***.

Stem cells are one of the most fascinating areas of biology today. But like many expanding fields of scientific inquiry, research on stem cells raises scientific questions as rapidly as it generates new research on stem cells is advancing knowledge about how an organism develops from a single cell and how healthy cells replace damaged cells in adult organisms. This promising area of science is also leading scientists to investigate the possibility of cell-based therapies to treat disease, which is often referred to as regenerative or reparative medicine ***(Till et al., 1961)***.

With more than 50 years of experience studying blood-forming stem cells called hematopoietic stem cells, scientists have developed sufficient under-standing to actually use them as a therapy. Currently, No other type of stem cells, adult, fetal or embryonic, has attained such status. Hematopoietic stem