was injected, the pain compression repeated, and this time the volunteer showed and reported no pain. The morphine and compression was repeated several times. Then, the volunteer was unknowingly injected with a saline placebo, but still reported no sign of pain, though the last time he was unmedicated the signs of pain were obvious. In a last test, the patients' 'morphine' was actually an injection of naloxone, an opioid antagonist. Even though the volunteer believed the shot was morphine and expected relief, the endorphins' effect was blocked by the naloxone injection and the volunteer displayed the same signs of pain as the first unmedicated trial.

In 1999, clinical researchers reported that inserting acupuncture needles into specific body points triggers the production of endorphins. In another study, higher levels of endorphins were found in cerebrospinal fluid after patients underwent acupuncture. In addition, naloxone appeared to block acupuncture's pain-relieving effects. However, skeptics say that not all studies point to that conclusion.

Apart from pain relieving endorphins are also produced on strenuous exercise when the threshold is crossed and produce a state of euphoria known popularly as "Runner's High". The good feeling one gets from an orgasm is partially attributed to the release of endorphins.

Thus understanding the physiology behind endorphin's gives us a wide scope in the field of management of pain. Surely a lot of advancement can be made in this field, and studies and research should be undertaken to *develop specific modules to counteract pain by stimulating deliberate endorphin releas*e. At present one fails to deal with this in an efficient manner due to lack of belief and high individual variations in pain perception and thresholds. But in coming years surely the mystery of placebo's in pain relief will be completely unveiled. The benefits of this modality to the patient as well as clinician will be unimaginable, as on one side it will relieve the patient from agony of pain and on other hand it will largely cut down the cost of management and cumbersome side-effects related to long term pharmaco-therapies.

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STEM CELL THERAPY AHEAD

Verma AP*, Patel JP**, Nirvan AB ***, Mod HS +

* M.D. (Physiology)
Asso.Prof.in Physiology, N.H.L.Municipal Medical College, Ahmedabad.
** M.S.(Anatomy)
Asst. Prof. in Physiology, N.H.L.Municipal Medical College, Ahmedabad.
*** M.S.(Anatomy),DNB(Anatomy)
Asst.Prof. in Anatomy, P.D.U. Medical College, Rajkot.

+ M.D.(Physiology)
Asst. Prof. in Physiology,N.H.L.Muncipal Medical College, Ahmedabad

STEM CELL THERAPY AHEAD

Abstract: The goal of any stem cell therapy is to repair a damaged tissue that can't heal itself .This might be accomplished by transplanting stem cells into the damaged area and directing them to grow new, healthy tissue. It may also be possible to coax stem cells already in the body to work overtime and produce new tissue. To date, researchers have found more success with the first method, stem cell transplants.

Introduction

Why don't we live forever?
Because we get sick?
Because we get old?
Because we get hurt & can't heal?
All these are correct. Each one results from a failure of the body's ability to grow, maintain or repair itself-functions that depend on our stem cells. For decades, researchers have been studying the biology of stem cells to figure out how development works and to find new ways of treating health problems.

Research has shown that cells originating in one organ can travel to another and assume the identity of cells at there new locations. This phenomena, called plasticity has been demonstrated in model organisms such as mice & rats as well as in humans.

Hierarchy of pleuripotency of stem cells:
Zygote: Totipotent, potential to generate all cells of different tissue to make whole organism.
Inner cell mass of blastocyst: Pleuripotent, ability to form all cell types present in the organism but cannot form whole organism.
Adult stem cells : Pleuripotent, usually differentiate along one lineage can show trans-differentiation (or heterokaryon formation)

Human cloning

2 major aspects of human cloning
1. Reproductive cloning :cloning for babies:-Banned by international treaty drafted by United Nations.
2. Therapeutic cloning to form stem cells from blastocyst inner cell mass for cell regeneration therapy

ETHICAL ISSUES RELATED TO THERAPEUTIC CLONING

Stem cells : Exciting to physicians ,scientist & patients
Challenge for Ethicists & Policy makers
Objections:

1. When does life begin?
2. Cloning –Creating of genetic replica?

3. Can blastocyst derived from SCNT be called embryo?
4. Use of oocytes: Issue of mitochondrial inheritance.

THERAPEUTIC CLONING USING STEM CELLS FROM VARIOUS SOURCES

Existing established cell lines of stem cells permitted for research only (Allogenic source).

Adult autologous cells converted into stem cells by oocyte fusion (SCNT) permitted for research with a long term therapeutic goal.

Adult stem cells:Trans-differentiation(Plasticity)

Sources of Stem Cells

1. Embryo's collected during IVF(SPARE embryos)-ESC
2. Embryos created by somatic cell nuclear transfer(cloning) – SCNT derived SC
3. Germ cells or reproductive organs of aborted foetus –GSC
4. Adult blood or umbilical cord blood
5. Bone marrow & other adult tissues –ASC
6. Somatic cells of aborted foetus.
7. Dormant cells obtained from model organisms or human.

MOLECULAR BASIS OF TRANS-DIFFERENTIATION OF ADULT STEM CELLS

1. Trans-differentiation (Metaplasia)-Irreversible switch of adult stem cells of one lineage to differentiated cells of other lineages
2. Associated with change in cellular morphology & reprogramming of gene expression
3. Caused by change in the expression of master regulatory genes, whose function is to distinguish between 2 tissues in normal development (master switch)
4. Master switch genes-mostly transcription factors

Trans-differentiation of BM-SCs

- Two SC populations in BM:

1) Haematopoietic SCs- Give rise to mature lineages of blood
2) Mesenchymal SCs-Give rise to bone ,cartilage, fat cells

Both of them can be induced to produce non- haematopoietic cell types:

Neurons, pancreatic cells, hepatocytes , muscle cells etc.

Is it a true trans-differentiation?

Is it fusion with target tissue cells to form Heterokaryons

- In this procedure, a nucleus from an adult donor cell is inserted into a recipient egg cell from which the nucleus has been removed. The nucleus provides all of the necessary genetic information, in the form of DNA, for a cell to function and divide. The resulting cell is then stimulated to divide as a zygote and it would results in the growth of embryonic stem cells that are genetically identical to the adult donor cell. Nuclear transfer, the transfer of a post-mitotic somatic cell

nucleus into an enucleated oocyte creates a limitless source of autologuos cells that when combined with gene therapy can serve as a powerful therapeutic tool.

Therapeutic cloning might be a viable approach to growing an exact tissue match for a patient in need - if the donor nucleus came from the patient, the resulting embryonic stem cell line would be a perfect match.

Researchers and physicians are working to design stem cell therapies that

- Are more effective and
- Reduce the invasiveness and the risk to patients

Today's stem cell therapies usually rely on cells that are donated by another person. This raises the possibility of donor cell rejection by the patient immune system. Now it is possible for a person to use a sample of his or her own stem cells to regenerate tissue, which would reduce or even eliminate the danger of rejection. How might this be done? Some possibilities include. Collecting healthy adult stem cells from a patient and manipulating them in the laboratory to create new tissue. The tissue would be re-transplanted back into the patient's body, where it would work to restore a lost function.

- Therapeutic cloning, as described in Creating Stem Cells for Research, might enable the creation of embryonic stem cells that are genetically identical to the patient.

- One less invasive way to achieve this goal would be to manipulate existing stem cells within the body to perform therapeutic tasks. For example, scientists might design a drug that would direct a certain type of stem cell to restore a lost function inside the patient's body. This approach would eliminate the need for invasive surgical procedures to harvest and transplant stem cells.

On the surface, the possibilities for stem cell therapy seem limitless. Couldn't we use stem cell technologies to replace any diseased or damaged tissue in the body? To answer this question, researchers must figure out the true potential and limitations of stem cells. Some questions currently being addressed include:

- How long will a stem cell therapy last?
    - The reason we age is because our cells do. If adult stem cells are used in therapies, will the tissues created from those cells age and malfunction more quickly? Scientists don't yet know how long different stem cell treatments might last.

- Can we ensure that stem cell therapies won't form tumors in the body?
    - Embryonic stem cells are naturally programmed to divide continuously and remain undifferentiated. To be used successfully in therapies, embryonic stem cells must be directed to differentiate into the desired type of tissue and ultimately stop dividing. Any undifferentiated embryonic

stem cells that are placed in the body might continue to divide in an uncontrolled manner, forming tumors.

- Avoiding tumor growth is crucial to the success of stem cell therapies. **Let's look at this in more detail.**

  In both embryonic and adult stem cells, improper regulation of genes can lead to uncontrolled cell division and tumor formation. This is a special concern with cells that have been cultured in the laboratory for a period of time, because they may regulate their genes differently than they would in the body.

  Why does this happen? Because most cells in our bodies are not meant to divide indefinitely, and none of them are meant to grow in lab dishes. Many tissues, such as blood and skin, rely on a renewal process that directs cells to stop dividing, differentiate and even die after a period of time. Proper direction comes in the form of signals from neighboring cells and the environment in which the cells live.

To make cells grow indefinitely in lab dishes, this process must somehow be put on hold. This is accomplished by feeding the cells with a liquid medium containing nutrients and growth factor proteins, which cause the cells to activate genes that promote cell division. In most cases, the regular signals provided by the cells' normal environment are not all present.

Not all cells respond well to this new living situation. Some will die, leaving only the ones that are better suited to an environment where indefinite growth is encouraged. After many rounds of division in a lab dish, the surviving cells may have changed so much that they are unable to respond to the signals in the body's normal environment. They may even have permanent changes in their DNA. Putting these cells back into the body is a risky proposal, because they are conditioned to continue growing rather than differentiating, possibly forming tumors.

Simulating the body's normal environments in the laboratory is one of the major challenges in stem cell research, and it is the focus of intensive research efforts around the world. Future therapies will rely on our ability to manipulate stem cells in a way that will be accepted as normal by the body.

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ROLE OF HUMAN CHORIONIC GONADOTROPIN TESTING IN DETECTION OF EARLY PREGNANCY VIABILITY AND Its COMPLICATIONS

DR. DINESH A RATHOD M.D.*, DR. NITA J NINAMA, M.D.**DR. JITENDRA PATEL, M.S.***

HUMAN CHRIONIC GONADOTROPIN (hCG)

HCG is a glycoprotein hormone composed of two dissimilar units, α and β, joined noncovalently. There are multiple forms of hCG in serum and urine samples in early pregnancy, including intact hCG (molecular weight- 36700) and its free subunits free α(molecular weight- 14500) and free β (molecular weight- 10000) free β Unit is degraded by macrophage enzymes and in the kidney to make a β subunit core fragment is the principal hCG-related molecule present in urine during pregnancy[1] intact hCG comprises approximately 70% amino acids and 30% sugar residues.HYPERGLYCOSYLATED HCG(H-hCG) is produced by Invasive cytotrophoblast and it contains significantly larger oligosacharides . H-hCG accounts for more than 80% of different forms of hCG detected in the week following implantation.61+9% of hCG forms in the week that follows the missing of the menstrual period and 50+4% in the following