

Stem cell research

Dr. Veerendra Kumar C.M.
MD., DNB.

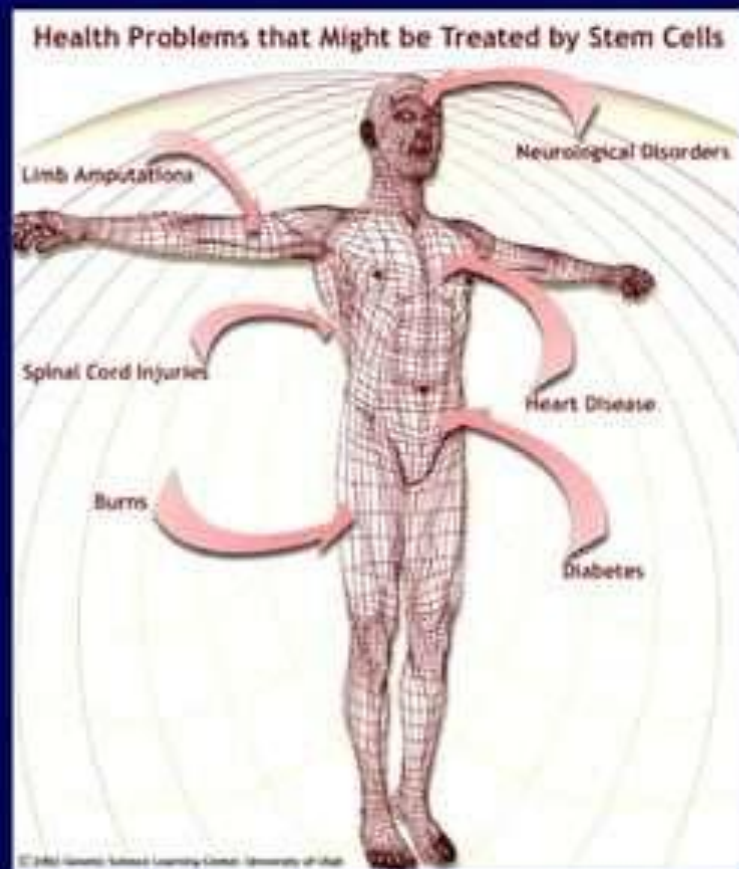
Associate Professor
VIMS, Bellary



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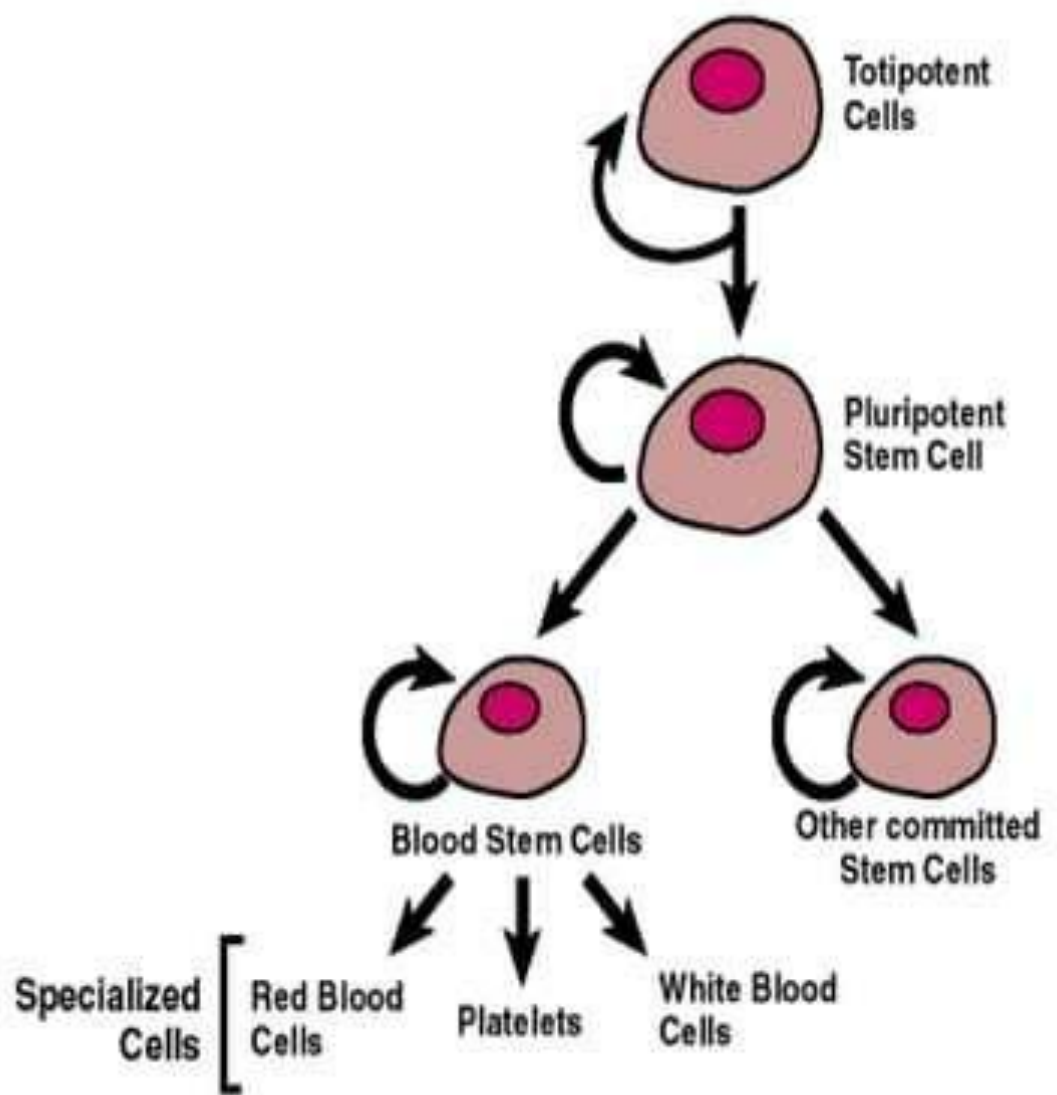
VIMS

Human suffering...



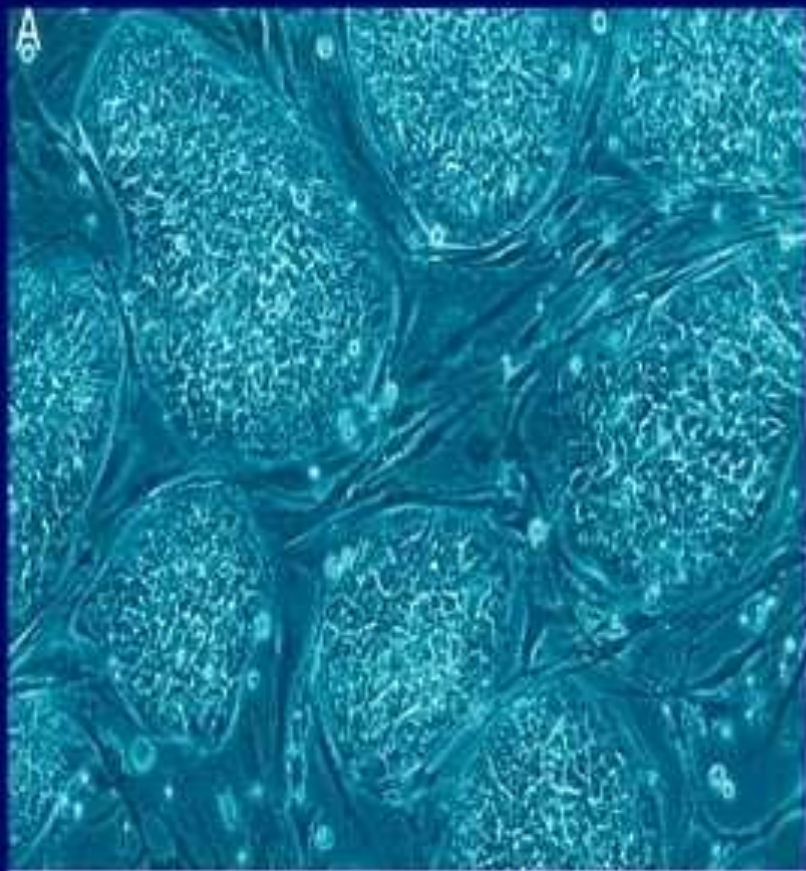
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- Totipotent
- Pluripotent
- Multipotent
- Oligopotent



What are stem cells?

- **Self renewal**
in undifferentiated
state
- **Potency**
to develop into
different cells



Regenerative medicine

- Study of early human development
- Therapeutic tool for various diseases
- Develop and test new therapies

hESC (human embryonic stem cells)

- To study drug toxicity-

liver cells & cardiomyocytes derived from
SC- useful to study drug toxicity

Davila ,Toxico Sci 2004;79:214-23

Types of stem cells



Adult - Bone marrow,
Cord blood

Embryonic - Unused IVF embryos
Pregnancy terminations

Embryonic V/S adult stem cells



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Embryonic stem cells (ESC)

- Embryonic cells are pluripotent and virtually immortal.



Fetuses from pregnancy terminations

- **Their ability to renew themselves is limited.**
- **Animal studies have shown that it is more difficult to produce normal tissues from these cells.**

Adult stem cells

- **A person's own stem cells should be the best source of cells for transplantation.**
- **Adult stem cells will eventually substitute for embryonic stem cells.**

Umbilical cord stem cells



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Adult Stem Cells and Postnatal Stem Cells

- Advantages
 - No ethical controversy.
 - None to minimal risk of immune rejection.
 - Reduced cost and time.
 - Genetic stability.
- Potential disadvantage
 - ?Limited plasticity
 - ?Limited lifespan in culture, may carry defective gene

FDA TRIALS USING ADULT OR CORD BLOOD STEM CELLS

- >70 current human clinical applications using adult stem cells
- there are no current human clinical trials involving human embryonic stem cells
- “It is nearly certain that the [human] clinical benefits of the [embryonic stem cell] research are years or decades away. This is a message that desperate families and patients will not want to hear.”

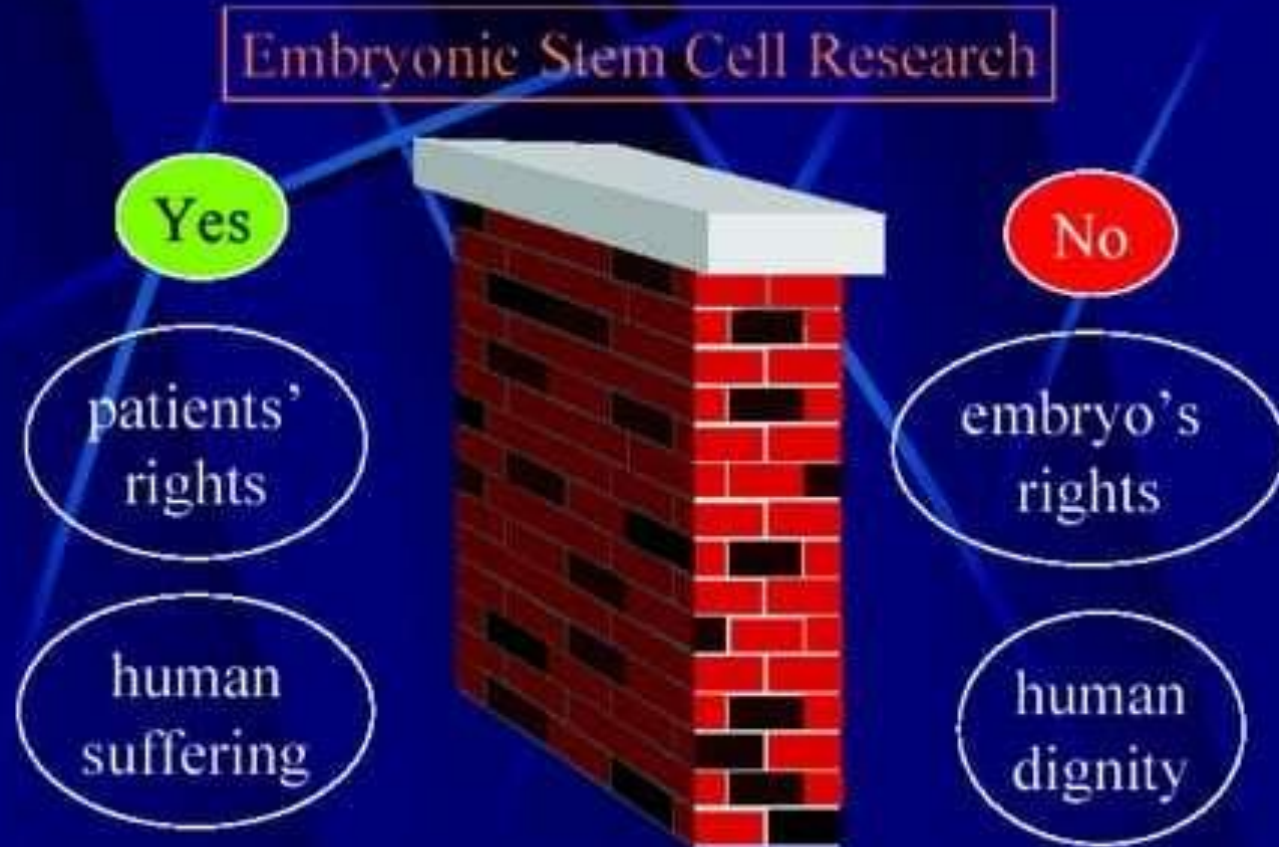
— *Science*, June 17, 2005

I DIED WAITING FOR
EMBRYONIC STEM CELL
RESEARCH TO FIND A CURE.
WHAT ABOUT YOU?

I WAS THE
EMBRYO



Debate over hESC



Objections and concerns..

An embryo should be accorded full human status from the moment of its creation

- A first step on a 'slippery slope' towards human reproductive cloning.



Conservative vs. Liberal

- Conservative = Literal Translation of the Bible
- Liberal = Compromising Translation of Bible



Question to consider:

Is it ethical to delay research

using embryonic stem cells until adult stem cells are fully capable of treating any disease?

Stem Cell Cultivation

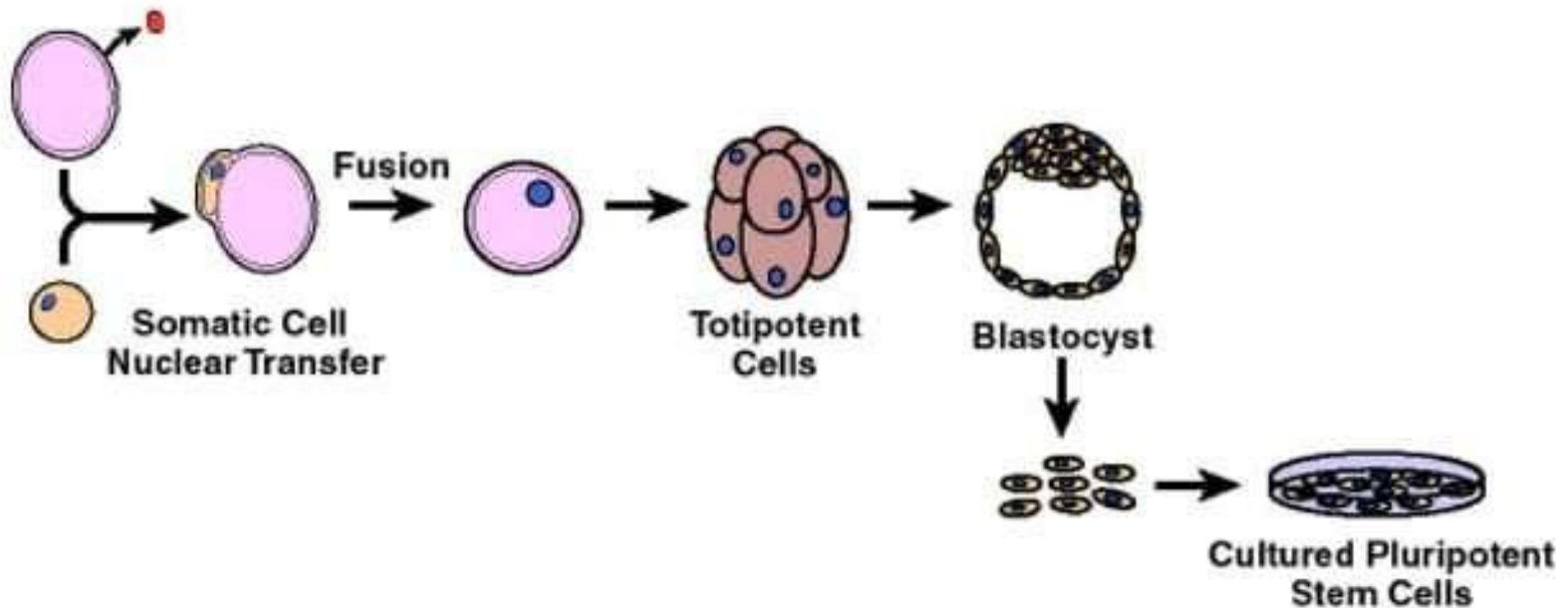


- 1 In Vitro Fertilized Egg**
- 2 Blastocyst Stage (5-7 days old)**
- 3 Inner Stem Cell Mass**
- 4 Cultured Undifferentiated Stem Cells**
- 5 Specialized Cells:**
 - a. blood cells**
 - b. neural cells**
 - c. muscle cells**

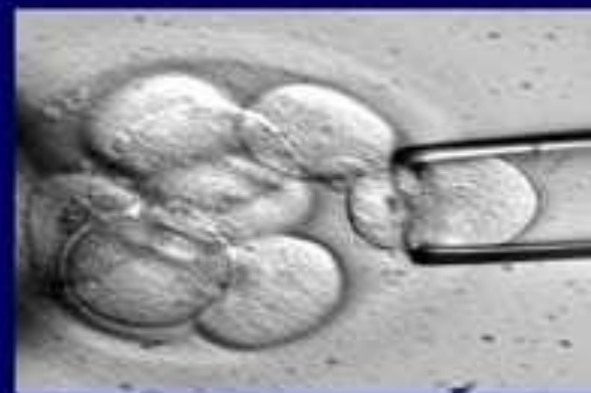
Somatic Cell Nuclear Transfer (SCNT)

technique used in 'CLONING'

May be ethically acceptable as you are not using embryos by conventional methods



Novel methods



- Extraction of single blastomere without damaging embryo and developed into independent hESC lines

Chung et al ,Nature 2006; 439:216-19

- Altered Nuclear Technique (ANT)
genetically modifying the somatic nucleus so that induced pluripotent stem cells are produced

meissener & Jaenisch Nature 2006;439:212-15

First clinical trial using hESC

- GERON Co, 2005-2006

Aldhous, Nature 2005;434:94-6

Existing lines of hESC

- 414 lines are available in 20 countries
- Characterization of these lines is limited
 - only 49% of lines are published in peer reviewed journals

Guhr et al Stem cells 2006;24:2187-91

Derivation of hESC

- Frozen embryos from IVF cycle

Expanded blastocyst – ICM
immunosurgical isolation

- Quality poor

-2nd quality embryos
-cryopreservation damages

Simon et al Fertil Steril 2005;83:246-9

Maintenance of hESC

- Immortal cells in undifferentiated state
- Optimal growth conditions for future therapeutic applications
- Majority of hESC have been isolated and maintained in fetal calf serum and mouse embryonic fibroblasts as feeder cell layers (Xenoproteins and xenosupports)

Problems

- Transmission of interspecies virus transfer
- Incorporation of foreign sugar molecule to hESC leading to immune response
- It may also lead to impairment of cell function & tissue development

Varki Am J Phys Anthropol Suppl 2001

Research focus is on....

- Use of human components instead of animal sources to avoid zoonosis
- Fetal, adult muscle tissue, skin, Fallopian tube, endometrium, foreskin cells
- Successful undifferentiated growth of hESC using xenobiotic –free feeder system

Richards ,Stem cells 2003;21:546-56

Research focus is on...

- Feeder free culture system from recombinant sources

Ludwig Nature Biotech 2006;24:185-7

Differentiation

- Direct hESC to differentiate into specific cell lines
 - drug development
 - cell replacement therapeutics
- Specific germ cell layers can be directed by adding specific growth factors

Scientific Stem Cell Challenges

- Stem cells represents a very small fraction of cells in tissue.
- Isolate a small number of stem cells (finding a needle in a haystack).
- Expand the number of stem cells for research and clinical applications.
- Maintain genetic stability in culture and in recipient.
- Culture media has to be free of animal protein.
- Deliver cells to tissue of interest.
- Stem cells have to be functional.
- Avoid or restrict tissue rejection.

Challenges to Stem Cell/Cloning Research



- differentiation to the appropriate cell type(s) *before* using clinically.
- Recently, chromosome abnormalities in three human ESC lines.

Challenges to Stem Cell/Cloning Research

- Stem cell development or proliferation must be controlled once placed into patients.
- Possibility of rejection of stem cell transplants as foreign tissues is very high.



Beware

- Private companies promising wonders with stem cells - mostly in countries with unregulated laws

Ilic D, Regenerative med 2006;1:1-4

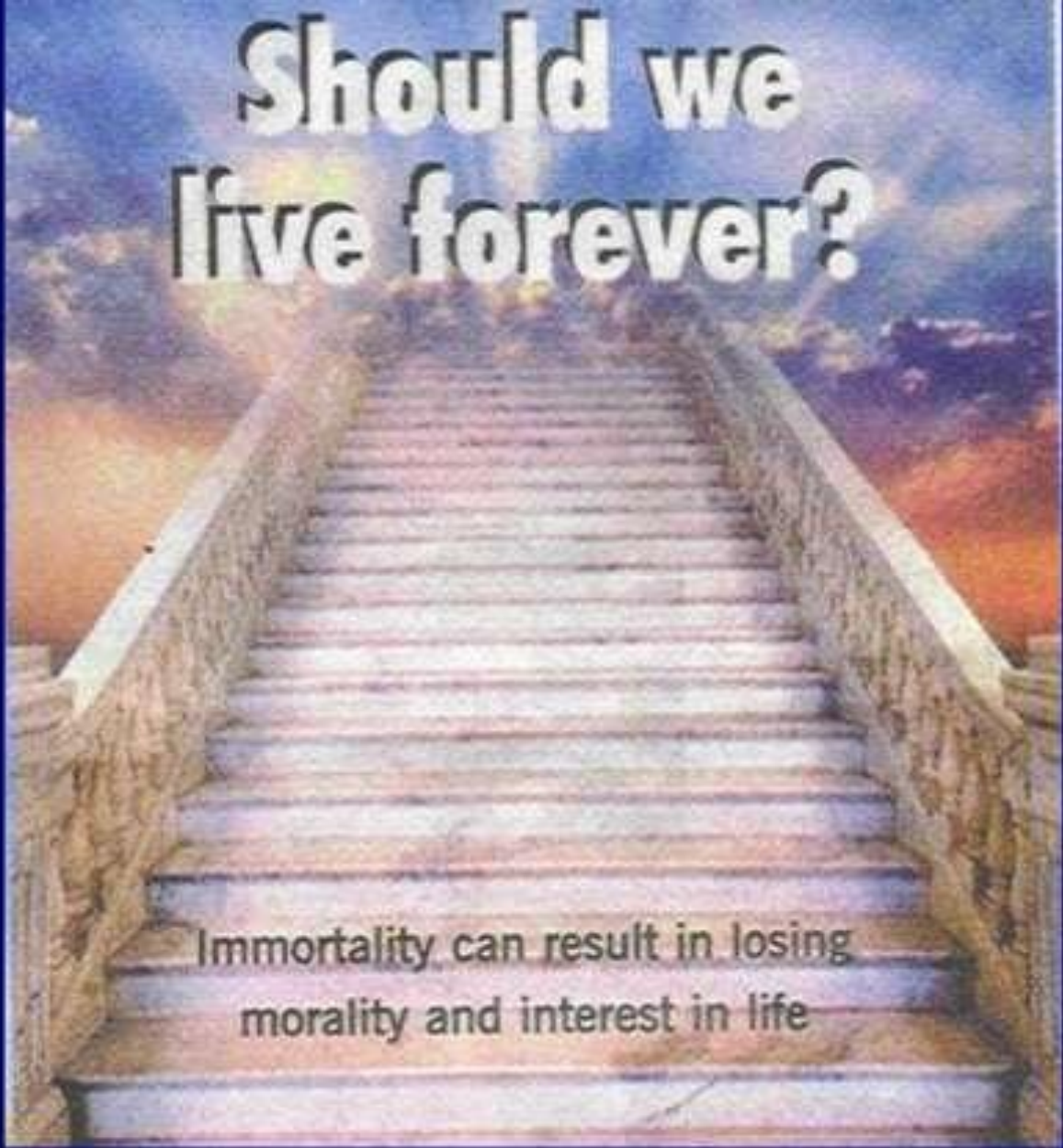
- UKRAINE –capital of ESC ?
but the references they quote do not have international authenticity in peer reviewed journals

Playing God



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Should we live forever?

A long, stone staircase with a decorative railing leads up towards a bright, glowing horizon. The sky is blue with some clouds, and the overall scene is illuminated by a warm, golden light, suggesting a sunrise or sunset. The staircase is the central focus, leading the viewer's eye towards the light at the top.

Immortality can result in losing
morality and interest in life