OPINION

CAN OR SHOULD HUMANS BE CLONED?

If a nucleus of an animal cell is transplanted (transferred) into an enucleated egg of another animal of the same species, then under the right conditions, the enucleated egg containing the transplanted nucleus would divide and eventually develop into an exact copy of the animal who donated its nucleus, i.e., a clone of the nuclear donor. Hence, the official designation of "cloning" is "nuclear transfer". A clone is thus an animal which has the same genotype and showing the same phenotype of another animal. Monozygotic twins are natural human clones. These twins have the same genetic make up and look exactly alike,

The first animal to be cloned is a frog. In 1952 Robert W. Briggs and Thomas J. King of the Institute of Cancer Research, Philadelphia, U.S.A., succeeded to clone the South African clawed frog (*Xenopus laevis*) by transplanting intestinal cell nuclei into enucleated eggs. When Briggs and King's work become public, scientists realized that someday, mammals and even human can be cloned. The first mammal to be cloned is a sheep In 1977 Ian Wilmut and co-workers at the Roslin Institute, Edinburgh, Scotland, announced the birth of Dolly, a sheep cloned from mammary gland cells. Dolly's birth was highly publicized, both by professional journals such as Nature and mass media magazines such as Times and Newsweek. Suddenly, the dream to clone humans seemed to be a step closer.

But should we clone humans? What benefit would it give to mankind? There are certainly possible instances where cloning could benefit people. One possibility would be for a childless couple with an azoospermic husband, where the possibility to obtain a child of their own is exactly zero. Cloning would help this couple to obtain an offspring who is genetically related either to the father (if the child is male) or the mother (if the child is female). Another possibility is for a couple in which one of the parents suffers from a dominant mutation causing a debilitating disease or a disease which would be fatal if not treated properly. Because it is a dominant mutation, all of their offspring would be affected. Gene therapy followed by cloning could help this couple to obtain a normal child.

The scenario would begin by an in-vitro fertilization. (IVF). The fertilized egg is allowed to divide several times, giving a clump of cells in some of which a healthy gene is introduced using one of the available gene transfer techniques. The nucleus of the corrected cell is then transferred into a fresh egg whose DNA has been removed. After a few cell division, the resulting embryo is then implanted into the mother's womb, and if all goes well, a healthy baby will be born. Still another possibility is a nuclear transfer not to obtain a clone but to obtain embryonic stem cells (ES cells). In this case, after nuclear transfer, the egg is allowed to develop up until the blastocyst stage, whereupon a mass of cells called the inner cell mass (ICM) is removed and cultured further giving rise to ES cells.

ES cells can be coaxed to differentiate into any differentiated cells, such as neurons, cardiac myocytes, and pancreatic beta cells. This will open the possibility to replace defective cells in people suffering from diseases such as Parkinson and Alzheimer's disease (neurons), cardiac infarction (cardiac myocytes) and Type 2 diabetes mellitus (pancreatic beta cells). Nuclear transfer to obtain ES cells is now known as "therapeutic cloning" to distinguish it from "reproductive cloning" whose goal is to obtain a clone. Even before it could be realized, cloning humans has raised a number of controversial issues, both technical and ethical. Cloning animal is allright, but cloning humans? What if it is misused, such as cloning criminals or as the case of a super-rich entrepreneur who maintains several clones of himself so that he can replace any of his organ if it fails?

Apart from the possibility of misuse, the main objection of reproductive cloning is its low efficiency. In Dolly's case, of the 29 embryos implanted, only one result in a live, healthy lamb, an efficiency of 3 % (1/29). Counting from the nuclear transfer done, the efficiency is very much lower, because the 29 embryos resulted from 277 nuclear transfer, an efficiency of 0.4 % (1/277). If the same applies to humans, about 300 oocytes would be needed just to deliver one baby. And how many recipient mother must be recruited?

Further more cloning may result in still-birth, and if it resulted in live-birth some of them dies within a few hours to a few days from unknown causes. Worst, Dolly herself, after giving birth to a normal lamb through conventional mating and gestation, has to be euthanasied a few years later because of untreatable respiratory trouble.

With this dismal track record do we dare to clone humans? As of now (2003) most countries put a ban on reproductive cloning at least until a better record in cloning mammals is achieved.

What about therapeutic cloning? The issue here is ethical rather than technical. Some people abhor the idea of creating embryos only to be killed later on to obtain ES cells, because embryos have the potential to become people and killing embryos will be the same as killing people. Others however, maintains that embryos are just a clump of cells that only become a sentient being until much later in development and thus cannot as yet be considered a person. Furthermore, leftover embryos from IVF procedures are routinely discarded and no body seemed to make a great deal of fuss about that (in fact one can derive ES cells from this discarded embryos).

There is as of now, no worldwide consensus on how to regulate therapeutic cloning and generating human ES cells. The spectrum of views range from allowing both therapeutic cloning and ES cells generation (United Kingdom, Singapore, Israel) through allowing generation of ES cells only (Netherlands and many other countries) up to forbidding both therapeutic cloning as well as generation of ES cells (Austria and Ireland)

As it turned out, the fuss about human cloning may be quite premature. Why? Because up till now no one has been able to clone monkeys, let alone humans. Although some workers have reported to be able to create Rhesus embryos after embryonic nuclear cell transfer, but for some reason none developed into pregnancy when implanted.

Turning to our country, what should we do in the field of cloning humans? As far as 1 know no regulation exists at present concerning both reproductive and therapeutic cloning. At the present state of the art, I would suggest that we should for the time being refrain from all attempts at cloning humans. What we could do is to derive ES cell lines from discarded embryos leftover from IVF procedures and use these cells to explore methods to derive somatic cells efficiently

Purnomo Suryohudoyo
Department of Medical Biochemistry
Airlangga University School of Medicine