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ISIS Report - 11/3/2001

Why Clone At All?

Why would anyone clone a sheep or a cow, let alone a human being? None save the genetic determinists who believe an organism is nothing more than the sum total of its genetic makeup and that it is their right to exploit cloned human embryos for spare body parts. **Dr. Mae-Wan Ho** explains why 'clone' is a misnomer. The original Dolly experiment was misguided, and subsequent attempts at cloning many other species have been plagued by the same failures. Far from producing identical copies of individual organisms, fatalities and monstrous abnormalities are generated at high frequencies. It is irresponsible and unethical to continue such gross experiments even for animals.

"Hundreds volunteer for clones"

An international team of fertility scientists gathered in Rome for a conference on human cloning amidst much controversy [1]. Since the team announced in January that they intend to produce the first human clone, some 600 and 700 couples have put themselves forward and the number is rising rapidly, according to team member Panayiotis Zavos, a US doctor. "Interest has come from all over, from Japan to Argentina, from Germany to Britain." He told reporters his team was ready to start cloning in the next few weeks, principally to help infertile couples, despite strong opposition from religious groups and from the scientists who are themselves involved in cloning animals.

Zavos said people would eventually get over the current opposition to human cloning. "Historically this is normal but once the first baby is born and it cries, the world will embrace it," he said. "Now that we have crossed into the third millennium, we have the technology to break the rules of nature." Have we?

Human cloning was contemplated at least as far back as four years ago when Dolly the cloned sheep was first unveiled. It is the ultimate eugenicist's dream or nightmare, depending on whether one subscribes to the mythical power of genes to determine fate [2].

A Frankenstein beyond reproach

On Sunday, February 23, 1997, Ian Wilmut, an embryologist working in the Roslin Institute just outside Edinburgh in Scotland, announced that they had succeeded in 'cloning' a sheep from a cell taken from the mammary gland of an adult. The clone, named 'Dolly', then seven-months-old, was said to be genetically identical to the adult from which the cell had been taken. Public reaction was swift. Did it mean this could be done in humans? Were we nearer to cloning human beings?

The headlines for the next few days were sensational. "Galileo, Copernicus -- and now Dolly!" . . . "The spectre of a human clone" . . . "In the past few days, we have lived through a change in our condition as momentous as the Copernican revolution or the splitting of the atom" . . . "Scientists 'able to create human clone' ".

President Clinton of the United States declared that the cloning of Dolly raised "serious ethical questions, particularly with respect to the possible use of this technology to clone human embryos." He told a panel of bioethics experts to report back to him in 90 days. (In June, Clinton imposed a ban on human cloning for 5 years.)

The story was on the front-page of the *New York Times*. It dominated television newscasts and gave rise to endless streams of articles and talk shows. By Wednesday, the share price for PPL Therapeutics, which carried out the work in collaboration with scientists at the Roslin Institute, had risen by more than a third, to increase its market value by £25m. We are to make no mistake as to what is driving the science. The Roslin scientists own no shares in the company, and will not benefit *directly*. However, the cloning technology has been patented jointly by PPL and the Institute. So the Institute will certainly expect to benefit from royalties, if not from continued research contracts and grants.

At first, the scientists involved dismissed cloning humans as science fiction. The technique was very difficult, they said. They had manipulated nearly 300 embryos to get one success. The fact that it could be done in sheep did not mean it could be done in humans. A few days later, Wilmut admitted that it could be done in humans, although the Director of the Roslin Institute, Grahame Bulfield, insisted they would not allow cloning to be used in harmful ways, and especially not for work on humans. Instead, he emphasised that the breakthrough could, in the long-term lead, to "a myriad new ways" to help humans. Herds of transgenic animals could be farmed for proteins, blood and organs. Gene therapy could provide cures for fatal diseases.

Ian Wilmut himself offered the prospect that a human embryo, produced by the same method, could be used to treat cancer and other life-threatening diseases. Human embryos would be grown until key cells could be extracted from the embryo and used to treat human diseases. During the work, the embryo would die. In other words, human embryos would be farmed, or ‘pharmed’ like the transgenic animals mentioned by the Director of the Institute. The horror of this thought was tempered only by Wilmut’s re-affirmation that cloning a human would be "technically difficult and ethically unacceptable". However, it transpired that patents on the technology filed by the Institute would cover all ‘animals’, including human beings.

A newspaper later in the year reported on headless frogs created by a scientist who raised the prospect of engineering headless human clones to grow organs and tissues for transplant surgery. He thought these headless human embryos could not possibly suffer, and would reduce public objection on ethical grounds.

While Wilmut welcomed Clinton’s reaction, and accepted the need for the issues raised to be considered by biologists and professors of ethics, he was unapologetic about the experiment. He expressed irritation at the continuing "atmosphere of criticism" surrounding his success. "Here we have a remarkable achievement, a world first, and there are people who seem to make a living out of spreading angst, he said. "You cannot blame the scientists for making those kind of discoveries. We are not Frankenstein-type people. If we hadn’t made the breakthrough somebody else would; the technology is out there. It is now up to society to decide how it should be used and we welcome any discussion of these matters."

These are significant words, not least because they reveal the scientist’s unspoken assumption that he can do no wrong. He is, by implication, simply following a natural obligation for the "advancement of science", an aim above reproach. In fulfilling this noble obligation, there can be no question of any personal responsibility to decide whether he should.

There were many forces at work that converge towards the cloning of Dolly. The pure motive of the advancement of science may be only one among them, personal advancement and prestige, a strong other. And one must not underestimate the importance of financial backing from the pharmaceutical industry, eager to reap the rewards of a growing market in reproductive biotechnologies. A substantial amount of the financial support for the research actually came from the taxpayer, via the Ministry of Agriculture Fisheries and Food.

Mounting pressure from industry and the scientific establishment eventually led to

legislation for ‘therapeutic’ human cloning, which was passed by the UK House of Lords in a decisive vote in January 22, 2001. While the legislation does not make reproductive human cloning legal, researchers in the UK can now create human embryos by the technique that made Dolly, for the purpose of providing cells and tissues for transplant purposes (see "The unnecessary evil of ‘therapeutic’ human cloning", this issue).

It is significant that not one among the luminaries invited to comment on Dolly in the UK within the first week of the discovery was a woman. Women have been conspicuously absent from the scene. The only allusion to women was Wilmut’s revelation that the world’s first cloned animal was named after the singer, Dolly Parton, because the cell used to create her came from the "impressive mammaries" of the adult sheep.

This ‘cloning’ technique is the latest in a long line of developments in industrialised societies that increasingly wrests control of reproduction away from women, to put into the hands of expert scientists and faceless corporations that turn reproduction into services and commodities.

It all began with the Pill and other methods of contraception predominantly aimed at women. Although the Pill is generally seen to give women more choice and control, it also puts the entire burden of responsibility for parenthood and otherwise on them, leaving men completely free and ‘blameless’. That is why we live in a society that still stigmatises single mothers. After the Pill came *in vitro* fertilisation and infertility treatments, sex determination of embryos, surrogate motherhood, germline gene replacement therapy, and now, ‘cloning’, a method that bypasses fertilisation altogether. It is the logical culmination of the instrumental, exploitative science that treats nature as so many objects to be manipulated for the benefit of ‘mankind’. So embryos, even human embryos, can be turned directly into commodities, or else into ‘pharm’ animals to produce proteins, cells or organs to order, for those who can afford to pay.

But who would want to clone a sheep, or a cow, let alone a human being? None save the genetic determinist who believe an organism is nothing more than the sum total of its genetic make-up and that it is their right to exploit cloned animals and even human embryos for spare body parts. It is indeed genetic determinism that inspires the act, that simultaneously validates and legitimises it and makes it so compelling, not only for the scientists concerned, but also for a substantial sector of the public who have become hooked on the genetic determinist propaganda.

‘A Human Triumph that Humbles Mankind’

A journalist, writing in one of the top newspapers in the UK, surpassed himself in the euphoria he experienced over the cloning of Dolly, "In the sheepish gaze of Dolly from Edinburgh, awesome possibilities glitter. We can imagine, just a little, how it must have felt to be a Tuscan Jesuit reading Galileo’s Dialogue on astronomy, or a pious Londoner settling down 250 years later with a first edition of *Origin of Species*." The reason for his euphoria was that he really believed geneticists have begun to reveal how much is determined in our genes, and that in gaining control of our genes, human beings are gaining control of their own destiny.

E.O.Wilson, the founder of the discipline of sociobiology that purports to explain all human behaviour in terms of the natural selection of genetically determined behavioural traits, was quoted in the same article describing the human brain (presumably human consciousness) as "an exposed negative waiting to be slipped into developer fluid". And, "The print is the individual’s genetic history, over thousands of years of evolution and there is not much anybody can do about it."

In the same vein, Jonathan van Bierkom, professor of genetics at the University of Colorado commented, "After all, if you believe in the selfish DNA theory -- the evolutionary imperative to propagate one’s gene -- then this is the ultimate." Richard Dawkins -- arch neo-Darwinian and genetic determinist, famous for the utterly banal idea that human beings are nothing but automatons acting under the influence of their ‘selfish genes’ whose only imperative is to replicate -- also declared himself delighted. He confessed he would like to be cloned. He would love to watch a tiny copy of himself grow up. "So instead of watching a mixture of yourself and your partner’s genes playing on the swings, you could watch the unadulterated you."

All too predictably, a letter in support of cloning, circulated on the Internet, was signed by among others, the three arch genetic-determinists: Richard Dawkins and E.O.Wilson, together with Francis Crick, famous for discovering the DNA double-helix and for propounding the doctrine of genetic determinism in its most extreme form.

"Now we can reproduce ourselves without sex . . . ", Andrew Marr continued triumphantly in his article, chiding both "religious fundamentalists" and "open-eyed liberals" for calling attention to eugenics (while admitting that they had a point), but citing with approval novelist Fay Weldon’s tongue-in-cheek comment that nature hasn’t done such a good job that we can’t improve on it, and that it is rather primitive of us to be so fearful of ourselves. It would definitely be a sin, he said, to use political authority to ban new thinking or new research. Tom Wilkie, a science journalist turned senior policy analyst with the Wellcome Trust charity, was quoted as saying that moral attitudes evolve and that, up until 1950, it was illegal and considered immoral to use the corneas of dead people for transplant.

If people like Wilkie and Marr cannot tell the difference between using human corneas for transplant and cloning a human being, then we have not only descended into complete moral relativism but have also substituted Science for God. There is an underlying attitude that Science is, indeed, beyond reproach, that it can never be wrong, while "moral attitudes" or ethics are infinitely negotiable and maleable. So, let us examine the science to see if it bears

out the claims that have been made for it.

How is the ‘cloning’ done?

In the ‘cloning procedure’, cells from an adult sheep’s udder are cultured until they reach a ‘stationary state’ and cease to grow or divide. A cell is taken from the culture and fused with an egg from another sheep from which the nucleus has been removed. This allows the nucleus of the cell, containing the genome of the first adult sheep, to substitute for the egg’s genome. The egg then starts to develop *in vitro* and, after making sure that it is developing normally, is transferred into the womb of a surrogate mother sheep that carries it to term. Out of a total of 277 embryos created in this way, only 29 developed sufficiently ‘normally’ to be transplanted into foster mothers. And of those 29, only one ‘Dolly’ resulted.

Actually, neither the idea nor the technique is new. Extensive experiments of this kind were done in the frog in the 1960s by John Gurdon’s group in Oxford, and the axolotl by other developmental biologists. *In no case, however, did the scientists involved claim they were creating clones. Far from it, for they knew they were doing no such thing.*

The intellectual motivation for the experiments came from a deep problem in developmental biology. Organisms, no matter how complex, typically start development from a single fertilised egg cell that goes through successive cell divisions to produce many cells. These cells then undergo a hierarchical process of determination to form different organs and, later on, to become progressively differentiated into distinctive nerve cells, skin cells, liver cells and so on. There are two related questions which nuclear transplant experiments address. First, when cells become determined to form different organs, does the process involve irreversible changes so that the cell loses the ability to form other organs and other cells? The second question is whether cell differentiation involves irreversible changes in the genetic material carried in the nucleus of the cell.

The scientific paper on Dolly published in *Nature* did not claim that Dolly had been cloned. It was entitled, "Viable offspring derived from foetal and adult mammalian cells". Cloning was claimed, however, in the press releases and official comments to the public. The implication of their claim was that the viable offspring, Dolly, contained the original "genetic blueprint" intact, and hence adult cells could be used to produce another organism like the original.

In the earlier amphibian experiments, many developmental abnormalities resulted, and the furthest any embryo resulting from the nuclear transplant developed was to the juvenile, tadpole stage. However, by repeating the nuclear transplant serially -- that is, taking cells from the first nuclear transplant embryo and transplanting the nucleus into a second egg cell -- it was found that adult frogs could be created, most of which were infertile and abnormal in some way. In one set of results cited, a total of 3546 nuclear transplants were done, using cells grown from adult frog skin. The success rate of the first transplants to produce tadpoles was 0.1% -- in other words, the failure rate was 99.9%. Serial transfers improved the success rate to 12%, but these tadpoles came from those 0.1% that had developed to tadpoles on the first transplant and were therefore pre-selected. And even the ‘successes’ showed varying degrees of abnormality.

The technique of nuclear transplantation was actually invented by two other scientists in the 1950s. Extensive series of experiments carried out subsequently led to the following conclusions.

- The developmental capacity of transplanted nuclei to support development decreases with the increasing age of the donor cells.

- The reduced developmental capacity of the nuclei is irreversible, and may involve DNA changes, such as chromosomal damage, as well as other alterations.

- The developmental abnormalities resulting from the nuclear transplants experiments show no correlation to the kind of cells used.

- There is no evidence that the original 'genetic blueprint' remained intact in any cell, except those obtained in the very earliest stages of development when the number of cells in the embryo could be visibly counted.

Thus, there is no evidence that the original 'genetic blueprint' remained intact in any cell, except those obtained in the very earliest stages of development when the number of cells in the embryo could be visibly counted. Nevertheless, in summarising their results, Gurdon stated, "The main conclusion to be drawn from the experiments summarised in this chapter is that the nuclei of different kinds of cells in an individual appear to be *genetically identical*." (my italics)

Gurdon's claim was not supported by the data, and contradicted the subsidiary conclusions made just before. This was surely someone trying to salvage the accepted dogma that genes (DNA) do not change in development, only the expression of genes, *in the face of evidence to the contrary*. This misreading or misinterpretation of evidence is familiar in the long history of genetic determinism [2].

The only real novelty in the Dolly experiment was that it was done in sheep, and that an apparently healthy live-birth was obtained without serial nuclear transplants. The interpretation of the results in the *Nature* paper was more cautious. Although it did not comment on the large proportion of failures, it stated, "The fact that a lamb was derived from an adult cell confirms that differentiation of *that* cell did not involve the irreversible modification of genetic material required for development to term" (my italics).

The science is seriously flawed

The science is fundamentally flawed in assuming that an individual is determined entirely by its genetic make-up and that the genetic make-up of adult cells remains unchanged. This is not supported by the results of the nuclear transplantation experiments. Many commentators in newspaper articles have pointed out, in the context of human cloning, that the clone is not identical to the original individual, on account of the different life experiences the clone will have. Even identical twins, which are more 'clones' in the strict sense of the word, are different individuals. However, there are other more specific scientific errors involved.

First of all, one cannot clone any organism simply from a cell taken from the adult organism. It cannot be done without the egg from the second sheep, which plays the key role in somehow 'rejuvenating' and 'reprogramming' the nucleus introduced with the cell, erasing all the 'imprinting marks' and other modifications in its DNA that make it a mammary gland cell. Most probably, the egg changes the introduced DNA in other ways so that it is appropriate to be the genome of a fertilised egg at the start of development. Recently, geneticists have come to suspect that one of the main reasons for the high failure rate of nuclear transfer cloning is because clones are not made from sperm and eggs, with their DNA properly imprinted by each parent [3].

Another important contribution of the egg cytoplasm is that it provides important cues for the proper body plan characteristic of the species -- something which is yet very imperfectly understood, despite the isolation of large numbers of genes affecting body plan in the fruit fly.

The egg also provides the food-store, as well as the sub-cellular 'power-houses' or *mitochondria* that generate the energy intermediate, ATP, which is used in all the energy transformations necessary for growth and development. The mitochondria, as it happens, have their own complement of DNA, and each mitochondrion with its DNA is replicated independently in the cytoplasm, so when the cell divides, each daughter cell will have the right number of mitochondria. Lineages of organisms can be traced through mitochondrial DNA, and mutations in mitochondrial genes are associated with a number of diseases. No cell can live without mitochondria.

The really interesting aspect of this experiment is the role played by the egg cytoplasm, which is almost uniformly ignored by all commentators, reflecting the patriarchal bias in current mainstream science. Nuclear-cytoplasmic interactions are well-known in the old scientific literature. Development cannot proceed if the nucleus and the cytoplasm are incompatible with each other. Many characteristics are so strongly influenced by the cytoplasm that 'cytoplasmic inheritance' used to be a subject in its own right before it was eclipsed by the general obsession with DNA since the 1950s.

Another scientific error is in assuming that the genetic make-up of all the cells in the adult organism is the same, and identical to the fertilised egg from which the adult has developed. This myth was already refuted by the nuclear transplantation experiments in amphibians, and finally exploded since the early 1980s by the discovery of the 'fluid genome'. Somatic cells (cells of the body apart from germ cells) accumulate point mutations and other changes -- insertions, deletions, rearrangements, duplications, amplifications and so on -- during the lifetime of the organism. Some of these mutations are implicated in cancer. These DNA changes may account for the low success rate of the cloning technique. Thus, it is a case of bad science to ignore, if not wilfully misread, the evidence.

Since the Dolly experiment, numerous attempts have been made to clone not only sheep but goats, cows, pigs, mice, and monkeys, with equally massive fatalities and abnormalities as well as excessive suffering inflicted on surrogate mothers who become mysteriously afflicted with fatty livers, fluid retention and other serious illnesses. From the known abnormalities in all the animal experiments, the scientists give a graphic description of what the first 100 human clones would be like [4]:

> "Almost all of the first 100 clones will abort spontaneously because of genetic or physical abnormalities, putting the health and lives of the surrogate mothers at risk. Of the handful of clones that make it to term, most will have grossly enlarged placentas and fatty livers.
>
> "And of the three or four fetuses that may survive their birth, most will be monstrously big -- perhaps 15 pounds (about 7 kilograms) -- and will likely die in the first week or two from heart and blood vessel problems, underdeveloped lungs, diabetes or immune system deficiencies.
>
> "With access to an intensive care unit, perhaps one of those 100 clones will survive, . . . It will bear the hallmark of most animal clones: a huge navel -- a remnant of the oversized umbilical cord that inexplicably develops during most pregnancies involving clones."

It is clear that cloning experiments are morally reprehensible if only for the suffering they cause, even in animals. We have had four wasted years in which enormous public and private resources have been squandered with no obvious returns in terms of scientific discovery or the health of nations. On the contrary, untold damage is being done to the social and moral fabric of civil society. It is time to draw a curtain over all cloning experiments.

References

1. "Hundreds Volunteer for Clones, Scientists Say" Jane Barrett, ROME (Reuters) 9 March 2001.

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3. McCreath KJ, Howcroft J, Campbell KHS, Colman A, Schnieke AE and Kind AJ. Production of gene-targeted sheep by nuclear transfer from cultured somatic cells. *Nature* 2000, 405, 1066-9.

4. "Cloning Humans: Failure Will Be the Norm" Rick Weiss *Washington Post* March 8, 2001.

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