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BY ---------- JNQUIRY INTO ASPECTS OF HUMAN CLONING

Introduction

Confusion exists concerning the meaning of the word *"cloning"*. The present comments are based on an operational use of the term which defines cloning as *"the copying of biological material using the biological mechanisms employed by cells andlor whole organisms ".*

Thus, the term may be used to encompass the replication of whole animals (including man) and plants, of whole cells and tissues (which may or may not have been subject to genetic engineering), or of portions of the instructional molecules determining cell function and structure known as the genome - so called DNA cloning.

Although there is overlap between these categories it is instructive to consider them separately.

Whole animal cloning

Various methods for cloning lower vertebrates (such as frogs) have existed for some time. Within the last 15 years or so these have been extended to mammals, notably to mice and more recently to sheep.

At first, the methods involved dividing up cells derived from very early embryos to produce identical individuals, all of which had originated from a single fertilised egg. More recently it has become possible to transfer the nucleus from a cell of an adult donor to an egg from which its own nucleus has been disabled.

Since this procedure can be repeated, the possibility of creating numerous clones of the donor adult now exists.

In general terms it is widely accepted that the cloning of a human being is unacceptable. If at all widely practised the exercise would constitute a gross extension of the discredited "principles" of eugenics current before the Second World War. Quite apart from this, current methods in animals involve a high failure rate and considerable risk of abnormal development. Even if it proved possible to adapt the technology to the human, the medical risks at present would be excessive.

It is, however, possible to imagine situations in which cloning procedures carried out to produce whole human beings might be considered socially acceptable. For example, a category of diseases result from abnormalities of replicating organelles known as mitochondria which are located outside the nucleus of fertilised egg cells.

Conceivably such conditions would be cured by transplanting an embryonic or adult cell nucleus into a previously enucleated normal egg cell. The resultant individual would, of course, have the genome carried by the nucleus, but would bear normal mitochondria.

It is necessary to consider these and similar situations in the context of whole human cloning - we do not serve the cause of humanity by closing our minds.

Clonine of cells and tissues

Most tissues of the body are derived by division and differentiation of undifferentiated precursors known as stem cells. In many cases such cells persist into adulthood and are responsible for the continued replacement of the tissue in question throughout life.

During embryonic development the various types of stem cell are themselves derived from more primitive (i.e. unprogrammed) precursors, since development itself is a hierarchical process. The most primitive stem cells (i.e. the original totipotent precursors of all the cells which make up the embryo) can now be isolated and grown in tissue culture conditions. Originally this cloning of so-called embryonic stem (E.S.) cells was achieved with cells derived from early mouse embryos, but there is reason to believe that true human E.S. cells can also be grown.

Pioneering work on mouse E. S. cells indicated that they can be induced by various treatments to differentiate into specific tissue types. Furthermore, they can be genetically engineered to exhibit desirable features such as the secretion of deficient hormones. Though in the very earliest stages of experimental development, this approach clearly has potential in attempts to produce replacement tissues and even organs in humans.

The origin of stem cells for human therapy is clearly a central issue here. Mouse E.S. cell lines are normally obtained from early embryos by a process involving the destruction of that embryo. The embryo at this stage is no more than an entirely undifferentiated ball of cells possessing none of the physiological attributes (such as nerve, muscle, heart) characteristic of a formed foetus or post natal individual. Nevertheless, ethical issues exist while at the same time the question of *"what to do with the spare embryos* obtained from some IVF procedures needs to be addressed!

More differentiated stem cells, i.e. those specific to individual tissues, might be cloned from embryonic, fetal or even adult tissues. Apart from some substantive work on blood and bone marrow, little has so far been achieved along these lines, since in most cases stem cells are difficult to identify and even more difficult to isolate in quantity. However, experimental work on animal tissues is likely to produce results which, in due course, would become applicable to human medicine.

DNA Clonin

DNA cloning has already proved to be of major medical importance. By introducing the appropriate DNA into micro organisms, it has become possible to induce the production

of human proteins in commercial quantities. Insulin, growth hormone and erythropoetin are examples of such recombinant therapeutic agents. Until the advent of this technology such materials were only available either from animal tissues, often in relatively small amounts, and with the risk of inducing an immune response with repeated administration, or else from human post mortem material with the attendant risks of delayed and potentially lethal cross infection.

The introduction of human genetic material into animal species, notably pigs, in order to make their tissues compatible with human tissues, is beginning to yield important results. The scarcity of human donor material and the increasing sophistication of such xenograft techniques suggest that this will become one of the growing points of transplant surgery. Immunosuppressants have deleterious side effects, notably an increase in the incidence of cancer following prolonged therapy. The insertion of human histocompatability antigens into potential donor species lowers the level at which such treatment is required.

In the future, DNA cloning techniques might also be used to introduce normal genetic material into the isolated cells of individuals suffering from a variety of congenital diseases, followed by their cloning and reintroduction to the body. Their subsequent ftniher proliferation would ameliorate or cure the underlying pathology. So far these attempts at gene therapy have not been successful, but they have good prospects of eventual accomplishment.