# DESIGNER GENES: GENETIC ENGINEERING AND EUGENICS.

CHRISTINE EWING. 1987.

In the past. fifteen years, massive scientific developments have taken place in the fields of recombinant DNA technology and genetic engineering. The year of 1978 saw the birth of the world's first "test-tube baby", and the technique of *in vitro* fertilization is now being applied to the "curing " of infertility in Europe, America, Australia, Asia and countries of the Third World. Even though these two areas of science *may* have seemed unrelated in their beginnings, the two have now converged. *In vitro* fertilization, the fertilization of egg with sperm in an external environment, provides embryos which may be re-implanted into a woman. It is still largely an experimental technique with a low success rate. Most women who go on IVF programmes will not give birth to live baby. These embryos are also the raw material which allow genetic experimentation and manipulation to be possible, by virtue of their external environment. The simultaneous development of DNA technology and IVF techniques has brought science and society to a unique point - the possibility of manipulation, and therefore gene therapy, to "correct" genetic disorders and diseases. Such therapy, if carried out on embryos, will affect future generations irreversibly, and this therapy inherently reinforces a discrimination against those who are differently abled in our society. It seeks to eradicate "defective" genes from future human populations.

In this chapter I will argue that what we are witnessing with the desire of scientists to genetically manipulate living organisms is the theory and practice of eugenics resurrected. Also, the increased emphasis to isolate the causes of diseases as genetic ones, to separate them from environmental factors, can be likened to the theories of sociobiology and biological determinism. Both eugenics and sociobiology have been used in sexist, racist and fashions, to reinforce prejudices, and to oppress certain social and ethnic groups. Evidence for the eugenic and determinist nature of genetic manipulation can be found in the basic scientific literature itself. Indeed, scientists have taken a great degree of licence in their writings to justify the possibility of gene therapy in humans. I believe that the *development of techniques* in molecular biology and IVF will provide the jusification for gene therapy, long before the ethics are decided. "If it can be done, it will be done."

Let us look at the recent history of the theory and practice of eugenics, and the theories of the science of sociobiology. Eugenics is a term first made popular by Francis Galton (the cousin of Charles Darwin) in 1883 in England, with the publication of "Inquiries Into Human Faculty and Its Development" (Galton, 1883) He took it form he Greek "eugenes", which means "of good birth". Eugenics claims to apply genetic principles to the improvement of mankind, and there are two general subdivisions:-positive eugenics - the increasing of the reproduction of fit individuals, and negative eugenics - reducing the breeding of unfit individuals (social degenerates, etc.). Galton thought that an individuals abilities and behavioural traits were genetically determined, and he was looking for the genetic source of his own family's genius (Alien, 1984).

In the beginning of this century, the eugenics movement gathered momentum in the United States, in both academic and popular circles, and it was associated with a sense of white Anglo-Saxon superiority and racism. It resulted in the passing of sterilization laws in 24 states for various "social misfits", for example, criminals, the mentally ill, sexual perverts, alcoholics, and others. In 1924, the Johnson Act was passed, which almost totally restricted immigration from Eastern European and Mediterranean countries into the United States (Allen, 1984). Eugenic writings and propaganda of the time, which influenced the passing of the Act, argued that white races were superior, and that intelligence had a biological and genetic basis. Characteristics such as feeble-mindedness and degeneracy were said to be inherited through single genes (Mendelian genetics). Later, many biologists withdrew their support for such arguments because of the scientific flaws and bias, but the immigration restrictions were not

repealed until 1965 (Allen, 1984). It illustrates the power that such arguments had, but also the reluctance by the law and the governments to denounce them. Racism essentially remained as an acceptable sentiment.

At a similar time in Germany, eugenic ideas were popularised under the term "racial hygiene", the first document appearing in 1895 written by a physician, Alfred Ploetz (Ploetz, 1895). Documents published by the Society for Racial Hygiene in the early 1920's stated that racial mixing was a dangerous practice, and that the white Nordic races were superior. Racial hygiene had become popular amongst the German medical profession, and the rise of Nazi-ism and Hitler saw the further embracing of purely biological values.

"No more than Nature desires the mating of weaker with stronger individuals, even less does she desire the blending of a higher with a lower race......

The Germanic inhabitant of the American continent, who has remained racially pure and unmixed, rose to be the master of the continent; he will remain the master as long as he does not fall a victim to defilement of blood."

#### (Hitler, 1925).

These values were institutionalized with the passing of laws. In 1933 the Law for The Prevention of Genetically Diseased Offspring was passed, and it meant that individuals with schizophrenia, feeble-mindedness, manic depressive insanity, genetic epilepsy, Huntington's chorea, blindness, deafness, physical deformity or alcoholism could be sterilized against their will. In 1935, the Law for The Genetic Protection of The German People disallowed marriage if one partner was genetically defective, Jewish, or from any race deemed "inferior". Doctors were also empowered to carry out euthanasia of people with "incurable illnesses". (Proctor, 1984). It is important to note that doctors and medical scientists were the chief exponents of racial hygiene in Germany. Of the 1300 members of the Society for Racial Hygiene up to 1930, most were physicians. The National Socialist Doctors Association, which represented the main medical wing of the Nazi Party, had more than 30,000 members in 1935, representing 60% of all. physicians practicing in Germany at that time (Proctor, 1984).

The science of studying social behaviour of animals is not new. However, in 1975, E. O. Wilson sought to establish sociobiology as a new field of study in his publication "Sociobiology: The New Synthesis". (Wilson, 1975). The theory of sociobiology asserts that all human behaviours, social relationships and organization are biologically, genetically, and evolutionarily determined. It says that human characteristics are explicitly programmed in our genes because they were adapted for survival, and the very existence of these characteristics proves it to be so, otherwise they would not have evolved. Sociobiologists claim to establish the innateness of wars, racism, competition, sex differences, and differences in social roles and positions. These theories have been used to justify, for example, the physical and social oppression of women. Sociobiologists can even explain the naturalness of rape! (Barash, 1979). Indeed, they can explain patriarchy as a naturally evolved order of society. Even though sociobiology has had several exponents in recent years, there are also critics who point out the deceptive and faulty methodology which is used - a kind of circular logic. Moreover, no evidence is provided for the existence of behaviour-causing genes (Bleier, 1985). In the context of human development, it seems impossible to tease apart genetic factors from environmental ones, but this is what sociobiology seeks to do - it ignores complexities in human development. As will be discussed later, there is an increasing trend in medical research to isolate *genetic* causes and separate them from environmental ones in human disease states, including those of a psychological nature.

The simultaneous developments in IVF technology and molecular biology have made gene therapy (the correction of "defective" genes to cure or ameliorate diseases) a forthcoming possibility.

But first, what are genes, and how do they act in living organisms, and how can they be manipulated?

Deoxyribonucleic acid (DNA) is the molecule of heredity in all living organisms. DNA is organised into structures called chromosomes inside cells. The normal complement of chromosomes in human cells is 23 pairs (diploidy), and gametes (ova or sperm) have half this number (haploidy). On fusion of an ovum and a sperm cell, the full complement of chromosomes is achieved. The discovery of the structure of the DNA molecule in 1953 by Watson and Crick lead to understanding the mechanism of how DNA replicates itself during the division of cells (1). This was the discovery that preceded modern molecular biology and genetic engineering - the overall structure was known, and thus it could be dissected into smaller parts.



DNA is a long macromolecule, consisting of two strands which intertwine to form a double helix.

Each strand is made up of smaller molecules called *nucleotides* (or bases) which occur in a defined sequence. Also, there is a set way in which bases in one strand of the helix can form chemical bonds with bases in the other strand, thereby holding the strands of the helix together. This is called *base pairing*.

A gene can be thought of as a piece of DNA within the chromosome which has a particular function. Genes act by determining the kinds of proteins (e.g., enzymes) that are made by cells for their necessary maintenance. The flow of genetic information in cells is as follows:-



Another type of nucleic acid, ribosenucleic acid (RNA) is made in the cell, using DNA as *template*. The sequence of nucleotides in DNA is used to make a strand of RNA. The sequence, or *message* in RNA is then used to make proteins, which are made up of individual amino acids, also in a defined sequence. The relationship between the sequence of bases in DNA and the sequence of amino acids in the corresponding protein is called *the genetic code*, and this code is exactly the same in all living organisms.

Some twenty years after the structure of DNA was postulated, the discovery of *restriction enzymes*, which can chemically cut DNA molecules at specific places, opened up the fields of recombinant DNA technology .gene "cloning", and genetic engineering (Emtage, 1985) DNA can now be broken into smaller pieces using these enzymes. It can be cut, manipulated and rearranged. Using such enzymes, particular genes can be isolated, and then

transferred to bacteria, where the gene is expressed and the corresponding proteon is manufactured by the bacterium. These techniques are known as *gene gene cloning*, since a particular gene can be amplified many times in this way. This is how human insulin was first manufactured in the bacterium *E. coli*. Isolated genes have also been transferred to mammalian cells grown in tissue culture. More recently, isolated genes from human or other species have been transferred to fertilized mouse embryos (or other species). The gene may be integrated into the chromosome and expressed in its new environment. These types of gene transfer experiments have provided the technical basis for the development of gene therapy, as well as the basis for a multi-million dollar, world-wide biotechnology industry (2).

Gene therapy aims to treat genetic diseases and disorders by replacing, the defective gene with a functional one. Some inherited diseases can be clearly traced to a mutation in a single gene, for example, B-thalassaemia, and these diseases are the most likely candidates for gene therapy. At present, there are two types of potential gene therapy. *Somatic cell therapy* involves the replacement of defective genes in the cells of one particular tissue of the body. Therefore, a functional B-globin gene could be transferred to bone marrow cells in order to correct B-thalassaemia (3). The second type of potential gene therapy is *germ-line therapy* where new genes would be injected directly into the embryo, obtained by IVF. All the body cells of this new individual, including its gametes, would theoretically carry the new gene. The gene would also be passed onto future offspring.

Recent developments in basic genetic research are improving the technical feasibility of gene therapy. While such therapy made *lead* to eugenic outcomes, it is clear from the scientific literature that the very rationale of these experiments has a eugenic nature - the aim is not only to "cure" disease - it is also to genetically alter the make-up of animals and humans, to get rid of "bad" genes. In the language of eugenics, it is to increase the reproduction of fit individuals.

*Transgenic* animals, particularly mice, are increasingly being developed and used as an experimental system to study how genes are expressed and regulated. Transgenic mice have had foreign DNA integrated into their germ-line cells, i.e., their gametes. This can be done by directly injecting an isolated piece of DNA into mouse eggs which have fertilized in the laboratory. The fertilized mouse eggs carrying the foreign DNA are then implanted back into pseudopregnant (superovulated) mice. This situation is exactly analogous to a human IVF experiment, excepting that human embryos have not been genetically altered (yet). The resulting new-born mice carry the foreign DNA in all their body cells (but perhaps to a variable extent). These mice are then be used for breeding, to transfer the foreign genes to subsequent generations (Palmiter and Brinster, 1985).

The earliest experiments of this kind were done more than 10 years ago (Jaenisch and Mintz, 1974), but the most noted and cited example was that where the gene for rat growth hormone was micro-injected into fertilized mouse eggs. Some of the mice that developed from these embryos expressed the new gene, and developed to twice the size of litter mates which did not carry the gene (Palmiter, et al., 1982). Putting new genes into embryos can also *cause mutations*. An experiment from Harvard Medical School reported the insertion of a mouse tumour virus joined to an oncogene (5) into mouse embryos, and the resulting offspring showed deformities of their limbs (Woychik, 1984). In other experiments, the *phenotype*, or physical appearance of transgenic animals was not altered, but nevertheless foreign genes were integrated into the chromosomes of embryos - this can be monitored by analysing the DNA in the offspring.

Some of the aims of this type of basic genetic research are to understand development processes in animals and how genes are expressed and regulated. For example, putting the genes for antibodies into mouse embryos and looking at how they are expressed helps towards an understanding of how the immune system in animals is regulated. Also, transgenic mice are being used to study how tumours develop (Palmiter and Brinster, 1985). However, scientists themselves advocate the application of these gene manipulation techniques to human gene therapy, and the barrier at present is that there is uncertainty as to how new genes behave, and whether they can be located to their correct site in the chomosome. Scientists are continuing to attempt to improve the techniques, to "target" genes to specific sites in chromosomes. They were able to selectively insert a B-globin gene into its correct position in the chromosomes of cells grown in culture. However, the context of the gene was different from that of the normal situation, and therefore the gene was not expressed correctly (Smithies, et al., 1985; Maniatis, 1985). The refinement of gene targeting techniques may allow more selective insertion of genes in the future, but how could all the possible random events that occur with gene insertion be controlled? Clearly, there are dangers and hazards, and in germline therapy, the new genes will be passed on to future generations. It is not a reversible process.

"Paving the way" for embryo manipulation is clearly an incentive among scientists for the further refinement of techniques in genetic manipulation. The designers of the "supermice" see greater possibilities:-

"This approach has implications for studying the biological

effects of growth hormone, as a way to accelerate animal growth, as a model for gigantism, as a means of correcting genetic disease, and as a method of farming valuable gene products."

(Palmiter. etal., 1982).

"Man has been interested in altering the genetic make-up of higher animals for thousands of years, dating back to the first primitive trials of breeding 'good' animals with other 'good' animals...... The approach of directly injecting genes into eggs currently offers the most promising technique for selectively altering the genetic make-up of an animal."

(Brinster and Palmiter, 1982).

In a review article of current gene transfer methods (citing 206 references!), the authors state that further sophistication of gene manipulation techniques "would help pave the way for embryo manipulation" (Kucherlapati and Skoultchi, 1984).

These statements contain eugenic intentions - to selectively alter the genetic make-up of animals, to select for "good" genes, to eliminate "bad" genes, to increase the reproduction of fit individuals. Although the experiments thus far have been done with animals, particularly mice, they have laid the groundwork for the justification for such experiments to be done with human embryos in the future, Are they *already* being done? *In vitro* fertilization is the vehicle for the externalization of embryos, which are then accessible for genetic manipulation:-

"So far, the experimental aims (of putting genes into early embryos) have been academic rather than practical but there is no reason in principle that this approach to gene therapy would not work in conjunction with *in vitro* fertilization."

(Williamson, 1982).

According to the same writer, the only reason that this principle is not yet the practice is a technical problem:-

"It is *our* (emphasis mine) inability to obtain correct to obtain correct gene function when DNA is put into a cell, and the fact that few inherited diseases affect only single tissues, such as bone marrow, makes gene impracticable at this time."

(Williamson, 1982).

Once the techniques have been mastered, gene therapy becomes practicable and therefore desirable! Some IVF doctors are also advocating this desirability to the point where IVF will become the best mode of childbirth because they could then ensure that no "defective" embryos would ever be re-implanted back into women. Helmut Zeilmaker of Rotterdam thinks that IVF will enable us to eliminate most genetic diseases within the next 25 *years*- He envisages a day when most people will reproduce using the egg and sperm from genetically screened individuals (New Scientist, July, 1986). Even though population control remains one of India's chief objectives, that country has also "embraced IVF technology". Dr. T.C Amand Kumar of the Institute for Research in Reproduction sees that IVF technology will have beneficial effects in medicine as a whole, especially in the treatment of inherited diseases by gene therapy (Jayaraman, 1986). The genetic analysis of the embryos to be re-implanted is taking on a major focus in current IVF research. Leading Australian IVF scientist. Dr. Alan Trounson maintains that while the primary focus of present IVF techniques is the treatment of infertility, genetic manipulation of embryos to overcome genetic disease is still on the agenda:-

"There are many more complex situations that *require* (emphasis mine) the development of sophisticated methods such as DNA insertion by techniques of genetic engineering to overcome genetic diseases and the sexing of human embryos for cases of sex-linked genetic disease".

# (Trounson, 1962).

The possibilities, and the intention, exist to select out which embryos will be used in embryo transfer. In previous times, laws have been passed to prevent the inheritance of undesirable genes. IVF and embryo manipulation is the combination which allows a new form of eugenics to be practiced. Not only are women's bodies used for obtaining the raw material - the stage is now set for the use of sex selection in association with IVF. Two British Medical teams have recently reported the development of DNA probes which can sex "preembryos" 4 to 8 days old. A member of the Edinburgh medical team. Dr. John West says that the probe was developed for the pre-natal diagnosis of sex-linked genetic disorders. He said that it wouldn't be ethical to use this test for sex pro-selection of babies. But, he admits, "we couldn't prevent the technique being used in that way" (Johnston, 1987). Again, the development of a technique by scientists has brought the possibility, and this time discrimination can be made on the basis of sex. We already know that in some countries, foetuses of the

female sex are aborted in their thousands (Congress: Women Against Gene and Reproductive Technologies, Bonn, West Germany, 1985).

Feminists have recognised previously that IVF provides the embryos necessary for genetic manipulation (Bartels, 1983; Minden, 1985). Some mainstream scientists are now be ginning to speak out against the excesses and eugenic possibilities of reproductive technology research. Recently, Jacques Testart, the leading French specialist in IVF, has denounced the continued development of IVF technology. Testart is worried about future perversions of this technique, such as the screening of embryos for genetic disease, or for the sex of a child.

> "If we have such techniques we can use them for many things. Eugenics is not far away. I think, it is better to abandon the technique than to take the risk."

> > (Nature, October, 1986).

However, Testart's fear that eugenics is not far away does not admit that the techniques are developed with a eugenic intention - they are designed for eugenic outcomes.

Other scientists too are beginning to speak out against the excesses of reproductive technology research. A recent commentary in the international science journal <u>Nature</u> by Professor Erwin Chagraff describes the "engineering of a molecular nightmare", in which the semi-industrial production of babies has arisen not from the demands of society, but from the will of scientists. The promise of financial gain is as prominent as the quest for knowledge of human reproduction. What is being unleashed is "a molecular Auschwitz, where valuable enzymes, hormones and so on will be extracted instead of gold teeth....... we can already see the beginning of human husbandry, of industrial breeding factories (Chagraff, 1967). These words paint vivid connections with the practice of eugenics, and Nazi-ism (6)

On other scientific fronts, there is a world-wide project to map the entire human genome. The original estimate of the cost of this project was 3 billion U.S. dollars, but estimates now stand between 50 and 100 million dollars (Lewin, 1987). This vast amount of money has been allocated to characterize every single gene in the human chromosome. Ironically, most of the DNA in the human chromosome does not code for proteins, and may have no apparent function. Is this worthwhile science, and what is the value of having such knowledge ? It seems to be a desire on the part of scientists and others with vested interests to understand human beings in terms of our "base sequences" There are increased efforts to locate the causes of diseases as genetic, without considering the interplay of environmental factors. Scientists are looking for the genes which cause cystic fibrosis, muscular dystrophy, Alzheimers disease (senile dimentia), and have branched into the psychological disorders such as manic depression. Researchers are attempting to identify these "disease-causing genes" by a process known as *reverse genetics*. Some genetic component is indicated through family studies of inheritance, but the responsible gene and its protein product are unknown. (for example, in cystic fibrosis there are no visible changes in chromosome structure). Reverse genetics involves the creating of many fragments of the chromosome using restriction enzymes, and then looking for particular sequences or "markers" which may be inherited along with the "disease gene".

The studies of manic depression (bipolar disorder) are important in highlighting the similarities with biological determinism, i.e., describing human behaviours as being genetically caused or determined. A study reported earlier this year has claimed that the gene *causing* manic depression is located on chromosome 11 (Egeland, et al., 1987). This particular study was carried out amongst the Old Order Amish population in the United States, the researchers say, because the genealogy of its 12,000 members can be accurately traced, they do not use alcohol or drugs, and the death rate by suicide attributable to the disorder is "easier to ascertain" because there are virtually no crimes of violence among the Amish population. However, even the initial diagnosis of manic depression suffers from a subjectiveness, because the symptoms are largely behavioural ones (7). The attempt to remove or disregard environmental factors is a similar approach to that used in sociobiology.

"Establishing the role of genetic factors in the aetiology of mental illness has represented a formidable challenge. The separation of environmental factors from intrinsic biological factors and the complexities of psychiatric diagnosis are major obstacles in this endeavour. Nevertheless, evidence of biological and genetic contributions to aetiology make the major affective disorders (8) excellent candidates to address this issue."

(Egeland. et al., 1987).

It is possible that an understanding of how manic depression is caused may lead to improved treatment of sufferers - it may also lead to a pre-natal diagnostic test. Researchers say that the stigma of manic depression will be removed if the cause can be identified as genetic (Kolata, 1987). The stigma of Trisomy 21 (Down's syndrome) or other disabilities have never been removed simply because the causes, genetic or otherwise, are known.

Would lesbianism or homosexuality DC more acceptable if a genetic cause could be found? Stigmas are about attitudes in our society towards those who are "different" - stigmas are not removed by finding genes to explain these differences. In fact, the stigma may increase and prejudices may be intensified.

Clearly, there are inheritable components in manic depression, but not everyone in "susceptible" families will develop the condition, and the existence of one responsible gene cannot be proven. Other studies of manic depression in Icelandic and North American families have found no linkage to chromosome 11 (Hodgkinson, et al., 1987; Detera-Wadleigh, et al., 1987), so even the genetics of this condition are multifactorial.

From the scientific literature on genetic research, the eugenic possibilities and intentions of genetic manipulation are evident. IVF and gene manipulation together constitute the new eugenics, under the guise of scientific progress. The purpose of gene therapy may on the one hand be to cure diseases - on the other hand, it is to prevent genetically-diseased offspring. This new eugenics is not very much different from the old, except that scientific techniques rather than laws have been used to give it form.

### <u>NOTES</u>

- (1) The discovery of the structure of DNA was attributed to James Watson and Francis Crick, who were given a Nobel Prize. It is less well-known however that the technical data of Rosalind Franklin were crucial to this discovery (Anne Sayre, 1975 "Rosalind Franklin and DNA." W.W. Norton and Co., New York).
- (2) Gene cloning in bacteria is being used to produce a variety of proteins with biomedical and therapeutic applications, e.g., insulin, growth hormone, blood clotting factor.
- (3) B-thalassaemia is a genetic disease where the gene for B-globin (part of haemoglobin) is damaged or missing. Haemoglobin is found in red blood cells and is responsible for carrying oxygen to the tissues of the body. In 1980, Dr. Martin Cline, of the University of California, attempted to treat bone marrow from two patients, using normal B-globin genes, and then carried out a limited marrow self-transplant. There was no previous basis that this treatment would give any clinical benefit. (Williamson, 1982).

- (4) Oncogenes are thought to be "switched on" in normal cells in the process of cancerformation.
- (5) Professor Chagraff is an Austrian who was forced to leave Europe by the rise of the Nazis.
- (6) The clinical symptoms of manic depression are mood swings. During the mania phase, patients are elated or irritable. They say that thoughts race through their minds. The patients exhibit increased activity and talkativeness. They have poor judgement and behavioural excesses. At other times, patients are clinically depressed, with feelings of hopelessness, and changes in their sleep patterns and appetite. They may have suicidal thoughts and actions (Kolata, 1987).
- (7) The major affective disorders are a group of illnesses manifested by disturbances in mood, and in physiological, cognitive and endocrine functions (Whybrow, et al., 1984)

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