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Genetic Engineering in 1990

*This paper seeks to review 'the state of the art' in genetic technology and look at key issues of ethics arising from their use on **nonhuman** life. A Christian approach to these issues is able to deal satisfactorily with them, involving Biblical principles of high respect for life and stewardship.*

***Key Words**: Cloning, Environmental release, genetic engineering, patenting of animals.*

A Christian Position?

Genetics strikes a deep chord as it involves changing ourselves and controlling the future generation of life. We have gained the ability to adapt our environment to our genes, and are now learning how to adapt our genes to the environment.

We are called to be stewards of the earth (Gen. 1:26, 28, 2:19; Ps. 8:6–8, 24:1). Stewardship is the proper use of human resources to change ourselves and the world and involves active participation in a responsible way, which should be a partnership with God. We must be humble, admitting the limitation of our finite minds and the perversion of motives caused by sin. Stewardship, however, involves creativity, with the obvious consequence that things will change.

There needs to be a balance between our creativity and caution. There is manipulation that improves, and manipulation which can harm.[1]

Mastery over nature should not be explored in a spirit of exploitation, but with reverence for all creation, as a gift entrusted to our care. God will judge those who bring ruin to nature and the earth (Is. 24:5–6, 45:18; Rev. 11:18). There is an amazing mixture of life. All is intertwined, in a delicate ecosystem which should not be needlessly disrupted. We could use the image of participation in the community of nature rather than domination of nature.[2]

Animals were part of the covenant relationship with man (Gen. 9:10, 5; Is. 50:2; Jer. 7:20). The Bible has often been criticised by nonChristian animal welfarists because of its assertion that man is uniquely made in the image of God, and has dominion over the rest of creation including the permission to kill and to eat animals. However, the belief that man is unique does not mean that animals have no rights, or better that we do not owe them duties. If we read our Bibles it is clear that we do have such

1 B. Haring, *Manipulation*, St. Paul Press, Slough (1975).
2 J. Moltmann, *God in Creation* SCM Press, London (1985).

duties (See eg. Ex. 23:4, 5, 10; Deut. 25:4, 22:6–7). In fact the Bible does teach a respect for all of creation. It was made for its own sake, not simply for man's needs and interests (Job 38:2–4; Ps. 8:3, 4, 19:1–6, 65:9–13, 104, 136:4–9, 148; Jer. 8:7). Being made in the image of God means that we should behave in a loving way as God does, who made animals not only for us, but for their own sake as part of creation. It is an issue of human responsibility which we cannot ignore. Animals cannot be viewed simply as expendable raw materials for our designs.

Potential of Genetics

Modern genetics and molecular biology have led to techniques by which it is possible to find the exact chemical sequence of any gene. A gene is made of a specific sequence of bases of DNA. The genotype of a multicelled organism is the complete set of genes they possess, and this is determined at the time of conception. It is normally the same in all cells of one individual organism. The exception is in chimeras, which are organisms made from at least two genetically different cells.

Enzymes called restriction endonucleases were found that cut DNA at short specific base sequences. DNA that has been cut into smaller pieces can be joined to other pieces of DNA. It can be incorporated into carriers called vectors, that normally multiply in the cell, and will also do so with any inserted foreign DNA. Recombinant DNA technology allows the earth's entire genetic resources to be exploited by providing a means of overcoming natural barriers of gene transfer. The technology has developed so that there are a very large number of different vectors. Many organisms can be 'engineered', and the range of possibilities has also increased with the large number of different genes which have been identified, sequenced and isolated.[3]

Industrial Application of Genetics

In the last decade genetically engineered bacteria and yeast have become common extensions of the long history of human use of microorganisms. Many human proteins can now be manufactured commercially by the use of these techniques, including the blood clotting factors, interferons, interleukins, growth hormone, erythropoietin, insulin and various growth factors, which have medical uses. Recombinant DNA techniques are also being used to produce vaccines against human or animal diseases. It would not be an overstatement to say that the new genetics is revolutionising the treatment of disease. More recently mammalian tissue culture cells have also been used to produce proteins. Bacteria have been made to produce enzymes for industrial use, such as lipase (enzymes that break down fat), which is now used to add to washing powders. There is also much work in the area of biopolymer engineering, involving the use of cells to produce

3 J. Marx, editor, *Biotechnology*, Cambridge University Press (1989).

polymers such as plastics. This involves transferring the genes that make natural polymers. It may save us using petroleum-based polymers, and allows much more precise control of polymer properties because it uses the precise enzymic design.[4]

Larger organisms are also being used to produce products. Transgenic plants are being used to produce industrial products, for example melanin, the natural pigment that darkens skin and has been made to be used in new sunscreen lotions.[5] There have been pharmaceutical peptides produced in oilseed rape plants, and even antibodies made in transgenic plants.[6] There are experiments underway to use animals to produce desired proteins in their milk, as protein factories or 'bioreactors'. Currently there has only been reasonable success using sheep which make human blood-clotting factor IX or human alpha-1 antitrypsin, though there is work on pigs, and cows. The advantage over bacteria is for proteins that require processing by mammalian enzymes after protein synthesis. The mammary gland is very useful here; for sheep about 400 litres can easily be collected per lactation cycle (in cattle the figure is 8000 litres), work is progressing.[7]

Commercial biotechnology is advancing into areas that depend on the introduction of genetically modified organisms into the environment. Bacteria and fungi can be made to degrade environmental pollutants. For instance the ability to degrade toluene has been transferred into bacteria that can live at zero degrees celsius.[8] There are other bacteria that can be used to extract and concentrate heavy metal contaminants from places such as land fills, mine tailings, or low grade mineral ores. Bacteria are already used to extract 10–20% of the world's copper supply.

Patenting of Life

Patents for individual molecules are held by different genetic engineering companies, similar to patents obtained for pharmacological drugs. The first patent obtained for a living organism was obtained after the court case Diamond v. Chakrabarty in 1980. Since then, many patents have been granted in many countries. The industrial competitiveness does lead to secrecy, but on the positive side the financial interest has created more funding, and faster overall progress in research.

The first patent to be issued for animals in the USA, applies to all non-human animals made containing an activated oncogene inserted by genetic

4 R. Pool, 'In search of the plastic potato,' *Science* (1989) 245: 1187–1189.

5 K. Buck, 'Brave new botany,' *New Scientist* (3rd June 1989), 50–55.

6 A. Hiatt, R. Cafferkey & K Bowdish, 'Production of antibodies in transgenic plants,' *Nature* (1989) 342: 76–78.

7 J. Van Brunt, 'Molecular farming: Transgenic animals as bioreactors,' *Biotechnology* (1988) 6, 1149–1154; A. J. Clark, *et al.* 'Expression of human anti-hemophilic factor IX in the milk of transgenic sheep,' *Biotechnology* (1989) 7, 487–492.

8 S. E. Lindow, J. H. Panopoulos & B. L. McFarland, 'Genetic engineering of bacteria from managed and natural habitats,' *Science* (1989) 244, 1300–1307.

engineering techniaues, and was based upon one such mouse made.[9] These animals, 'Oncomice' are being sold as research 'materials' for testing sensitivity to carcinogens, at US$50 an animal. The question of the patenting of animals is very contentious, and there have been some major studies on it.[10] Existing regulations can be adapted for most of the practical considerations of animal patenting, such as whether farmers should pay royalty fees for breeding patented livestock, but the ethical question is still unresolved. There are objections because animals have a higher status than nonliving matter, fears that it could lead to disrespect for nature, and that it will adversely affect small farmers who might not have access to the new varieties. Property rights have a long history of recognition in breeding animals, such as prize bulls and racehorses. However, the European patent office in Munich has turned down the application for a European patent for 'Oncomouse'. The legal situation varies between countries. In Europe microorganisms are patentable, but 'plant or animal varieties or essentially biological processes for the production of plants and animals' are expressly barred.[11] This is still being contested.

It is important that patenting protection does not prevent the widespread application of important new strains for scientific research and agriculture. Many companies are involved in the work solely for the fortune that they will make from using what are essentially natural genetic resources, which are merely moved around. There has to be some limit to how the patents are enforced, especially in areas such as agriculture where companies could be seen to be making a profit from the world food shortage. There must also be concern that large companies do not exploit third world natural resources, that they are gathering in the form of seed banks, at the expense of the people in those countries.[12]

Plant Breeding and Agriculture

The welfare of humanity is inextricably bound up with efficient agriculture. There are dozens of examples of agriculturally important genes and traits transferred to crop plants by interspecific or intergenic hybridisation using selective breeding,[13] but recombinant DNA technology allows the transcendence of inter-species barriers and makes very novel genetic combinations possible. There are several methods of gene transfer. The bacterium *Agrobacterium* is naturally found in associations with certain types of plants, and it can be used to transfer genes to those plants. Purified

9 Editorial, 'Towards the patenting of animals' *Nature* (1989) 336, 293 & 300.
10 U.S. Congress Office of Technology Assessment, *New Developments in Biotechnology-Patenting Life*, Washington: U.S.G.P.O., OTA-■-■, (March 1989).
11 European Patent Convention, Article 53(b).
12 C. Juma, *The Gene Hunters. Biotechnology and the Scramble for Seeds*, Princeton University Press (1989).
13 C. S. Gasser & R. T. Fraley, 'Genetically engineering plants for crop improvement,' *Science* (1989) 244, 1293–1299; R. M. Goodman *et al.*, 'Gene transfer in crop improvement,' *Science* (1987) 236, 48–56.

DNA can be used directly for plant transformation either by direct DNA uptake, such as by electroporation, by microinjection or by particle gun technology. The advantage with direct gene transfer methods is that they are not limited by the host range restrictions of biological vectors such as *Agrobacterium*. Transformation frequences of 1% are currently obtainable, and potentially any crop is now accessible.

The agriculturally important genes transferred include genes for insect and disease resistance. Herbicide-resistance genes from bacteria for the herbicide glyphosate (Roundup), Basta and other herbicides have been expressed in higher plants. Tobacco, tomato and potato plants have been bred which are tolerant enough to grow with concentrations of the herbicide that would kill all weeds growing alongside. Field trials have been underway since 1986 on these plants, and they will soon be commercially available. Tobacco plants resistant to tobacco mosaic virus infection have been bred. There are also plants that contain a bacterial toxin gene to make them pest resistant, the insect pests will die if they eat the plants. Monsato and Plant Genetic Systems, two U.S. Companies, have used toxins from the bacterium *Bacillus thuringiensis*. They put the toxin gene into tobacco and tomato plants and this protected the plants from the larvae of tobacco budworm.[14] Only those insects which eat the plants are affected, which is an advantage over chemical pesticides.

Plants will be able to be more resistant to drought, salinity or sensitivity to heavy metals, or less dependent on nitrogen fertilisers, so that they can be grown in areas of the earth currently unable to be used for agriculture. The food content of seeds, and plant products can be altered to improve the nutritional qualities. Tomatoes have been made whose fruits soften more slowly than usual, so that they last longer in shops.[15] There is the potential to make more nutritious plants, such as by increasing the level of the amino acid methionine in Soyabeans.

There are already many types of agriculturally important plants that have been grown with genetic modifications. The list in early 1989 included alfalfa, apple, *Arabidopsis*, asparagus, bananas, cabbage, carrot, cauliflower, celery, corn, cotton, cucumber, Douglas fir, flax, horseradish, lettuce, lotus, *Medicago varia*, Morning Glory, Orchard grass, peas, pears, petunias, pinetrees, poplar, potato, rape, rice, rye, soyabean, sugarbeet, sunflower, tobacco, tomato, trefoil, *Vigna aconitifolia*, walnut, white clover, with many to join.[16] We need to be able to feed a growing population and these additions to agricultural productivity will aid this. Environmental pollution is becoming a key area, and if we can avoid

14 U.S. Congress Office of Technology Assessment, *New Developments in Biotechnology-Field Testing Engineered Organism, Genetic and Ecological Issues*, Washington: U.S.G.P.O., OTA-BA-350, (May 1988).
15 M. Kramer, R. E. Sheehy & W. R. Hiatt, 'Progress towards the genetic engineering of tomato fruit softening,' *Trends in Biotechnology* (1989) 7, 191–194.
16 M. Ratner, 'Corp Biotech '89,' *Biotechnology* (1989) 7, 337–341.

excessive fertiliser and pesticide use we will also aid agricultural production. It is not so much the quantity of food that we can grow, but the way that we grow it, that is important.[17]

Animal Breeding

In the past, animal breeders have had to rely on the opportune use of stud animals which show the desired qualities, using selected mating, by natural or artificial insemination or *in vitro* fertilisation (IVF) and embryo transfer. Genetic techniques are being increasingly used to alter animals in both medical and agricultural research, and are being extended into many applications.

Genetically engineered animals are becoming the preferred source of experimental animals, seen in the growing number of transgenic animals made. Part of the reason for this is that scientists prefer to use standardised animal strains for experiments, and in the pursuit of knowledge they want to study the affects of genes not just on cells but whole animals. The effects of altering the genes will only be known inside the transgenic animals, and may be complex. New strains have been made already that are diseased, and feel more pain, and the question has to be asked whether it is right to breed them.

The first method used was to inject large quantities of DNA containing the chosen gene into fertilised eggs. The first publicised examples of this were mice that had multiple copies of rat growth hormone genes, some of which grew up to double normal size, later called 'supermice'.[18] This technique has been improved by the use of more targetable vectors such as retroviruses to give better control of integration. Another technique used is to use heat shock to induce triploid salmon which do not spawn, but continue to grow.[19] In mid 1989 it was found that it is possible for sperm to uptake DNA, thus opening the way for making transgenic animals by the sperm instead of by the eggs.[20] This would avoid the need for specialised micromanipulation that is needed for microinjection of eggs, but has been difficult to confirm.

The technique which people still associate most with the subject of cloning is that of nuclear transplantation. This is the technique that was used to make clonal frogs thirty years ago, and involves the transplantation of nuclei from a multicelled individual (which may be embryonic or more mature) into the enucleated egg cells. One way of removing the influence of the recipient cell's DNA is to irradiate them. This method was used in

17 P. R. Crosson & N. J. Rosenberg, 'Strategies for Agriculture,' *Scientific American* (Sept. 1989), 78–85.

18 R. D. Palmiter, *et al.* 'Dramatic growth of mice that develop from eggs microinjected with metallothionein-growth hormone fusion genes,' *Nature* (1982) *300*, 611–615.

19 OTA (note 14), p. 131.

20 M. Lavitrano, *et al.* 'Sperm cells as vectors for introducing foreign DNA into eggs: genetic transformation of mice,' $it *Cell* (1989) 57, 717–723.

making clones of salmon.[21] The sperm were irradiated before fertilisation, so that the sperm's genes are destroyed, but the sperm still stimulate the eggs to complete division so allow fertilisation to occur. The fertilised eggs were treated by pressure and temperature resulting in 90% clones. The purpose is to increase the number of females in the farm. Males can be produced by treating the hatched fry with a male hormone, so despite being chromosomally female about 80% of those treated could function as males. This technique has proved very difficult to apply to mammals. It appears that for proper development of mammalian embryos, genes from both parents are needed, as genes are differentially used from paternal or maternal chromosomes. More success has been achieved with fusions of whole embryonic cells, after embryo splitting.

The cloning that has been reported for mammals involves the splitting of preembryos into two or more preembryos which can then develop into several clones. Cattle, horses, pigs, sheep and mice have been developed from as little as a quarter of an embryo. Development and the ease of manipulation may be species dependent. There are related alternatives that can produce up to ten clones.[22] There are commercially available kits for 'do-it-yourself' embryo sexing and splitting (taking about three hours to use).[23] This type of technique is useful for agricultural breeders to rapidly increase the number of a breeding stock. The use of embryo transplantation is growing to be more common than artificial insemination for agriculture, and is becoming similar in price and success rate. It is possible to buy pairs of frozen beef cattle embryos for US$70 (including implantation). Dairy farmers are able to implant the embryos into their dairy cattle so that they can give birth to beef calves, which are worth more money, yet maintain the requirement for dairy cows to have a calf each year to maintain the high milk production.[24]

One of the most publicised outomes of embryo splitting was the creation of the sheep and goat hybrid, the so-called 'geeps'.[25] The hybrid chimeric embryo obtained from mixing sheep and goat embryonic cells developed into 'healthy' hybrid adults, displaying a mixed physiology and behaviour. A chimeric animal can occur naturally. Some chimeras will not develop as they are rejected by the mother's womb. This may be overcome by only substituting foreign cell into the inner cells mass, leaving the trophectodermic shell around the outside of the embryo, which develops into the placenta, to protect the new embryo. This has led to sheep being able to give birth to goats, and vice versa. This type of embryo transfer

21 B. Johnstone, 'Japanese Solve Riddle of Salmon-Cloning,' *New Scientist* (Nov. 3rd 1983), 328.

22 S. M. Willadsen, 'Nuclear Transplantation in Sheep Embryos,' *Nature* (1986) *320*, 63–65.

23 L. Glasgow, 'Kit for sexing embryos sets to work down on the farm,' *New Scientist* (9th Dec. 1989), 19.

24 P. Newmark, 'From the dairy case to the butcher block,' *Biotechnology* (1988) *6*, 1281.

25 C. B. Fehily, *et al.* 'Interspecific chimaerism beween sheep and goats,' *Nature* (1984) *307*, 634–636.

technology may also be very important to preserve rare species, by using domestic animals as surrogate mothers. These chimeras are used for the study of cell differentiation and interaction in the developing and mature organisms.

One major development in embryonic manipulation and genetic engineering is the use of embryonic stem (ES) cell lines.[26] These ES cell lines are established in culture from preimplantation blastocysts and can colonise both the somatic and germcell lineages of chimeric animals following their injection into host blastocysts. ES cell lines have made genetic manipulation much easier. These cells can be grown in cell tissue culture *in vitro*, genetically manipulated, the desired transformed somatically growing ES cells selected, and only these cells used to make chimeric embryos which when born give rise to new strains of mice. Many mutations have been made in different genes, resulting in the generation of new strains of animals. Animals can be made as experimental models of human disease, for example the first mice strains that are deficient in an enzyme HPRT were made as potential animal models for the human disease Lesch-Nyhan syndrome.[27]

Applications for Animal Use

Of obvious commercial value is the ability to control the sex ratio of offspring in breeding populations of livestock. It is possible to alter the sex balance of food animals, as described for salmon. There are several methods that claim to separate semen into X- and Y-bearing sperm (there are two sex chromosomes in mammals, X and Y, the female genotype is XX, male is XY, and the sex is determined solely by the sperm). There is still much research, and it appears that there are male-specific antigens expressed in 8-cell embryos of mice, cattle, pigs and sheep that can be identified. When it is known that these methods do not damage the progeny, they will be used for human sperm selection which currently can only alter the natural sex ratio by a factor of two. It is also possible to use embryo sexing, by analysing the DNA of a single cell out of an eight cell embryo, and only implanting embryos of the right sex or other genetic characteristics. Embryo sexing at any time after the eight cell stage is already being performed for humans as well, though it is aimed at avoidance of sex-linked genetic disease.

The type of genetic alteration that could be used includes improving the weight gain, disease resistance and fertility. There has been success making vaccines using gene technology, for example a vaccine made by workers at the C.S.I.R.O. in Australia against the external cattle parasite tick, *Boophilus microphilus*. Genetic engineering is being applied to farm animals,

26 M. R. Cappecchi, 'Altering the genome by homologous recombination,' *Science* (1989) 244, 1289–1292.

27 M. R. Kuehn, *et al.*, 'A Potential Animal Model for Lesch-Nyhan Syndrome though Introduction of HPRT Mutations into Mice,' *Nature* (1987) 326, 295–298.

such as sheep, cows, chickens, pigs and fish, with the goal of increasing their growth rates by introducing extra growth hormone genes.[28] The enhanced growth of mice after transfer of the human growth hormone gene is an effect that is being repeated in other animals, though only effectively in fish. Pigs that are being tested, were found to grow more rapidly but have a high morbidity.[29] There needs to be a deeper understanding of the genetic regulation. The way that animals respond to new genes will only be known after experiments on them. The aim is not to make larger animals, but faster growing ones. The way the over-expression of an exogenous gene such as that for growth hormone affects the complex processes regulating growth rate, body composition and reproductive characters can only be discovered by experiment. There is consumer opposition in some countries to meat produced in animals made to grow faster by injections of the protein, growth hormone, and Europe has refused some American beef imports because of this. Public attitudes may change, but are another factor. Any food products must be shown to be safe for their intended use.

Military Applications

One unethical use of these techniques that is of grave concern is their major use in the military sphere, although biological weapons are outlawed by a Geneva convention. This research is claimed to be defensive, but there is really no distinction from offensive, as in order safely to commence germ warfare one should be immune to what one is releasing. It is very easy to engineer toxic bacteria, e.g., the genes controlling toxins such as those of cholera or botulinus can be put into the normal human intestine bacteria *E.coli*. Numerous more lethal combinations have been constructed.[30]

Mixing Genes of Different Species

Our Christian view of creation means that it exists for God's glory. It has a meaning and worth beyond human utility. It has intrinsic value. Preservation of each species is important (Gen. 9), so we should not lose each species' identity, but the question of changing the genetic identity is harder to answer. There is a law in the Old Testament (Lev. 19:19), which says not to crossbreed animals or plant two plants in the same field. This verse is not considered relevant to the field of modern genetics or agriculture. As we discover how information has interchanged freely it becomes even less 'unnatural'.

The argument against genetic manipulation that we should not cross species barriers is weak. Nature has set barriers to horizontal gene transfer in eucaryotes, but trans-species gene exchange by a process called conjugation is common among procaryotes. There has been little investigation of

28 R. Jaenish, 'Transgenic animals,' *Science* (1988) *240*, 1468–1474.
29 V. G. Pursel, *et al.*, 'Genetic engineering of livestock,' *Science* (1989) *244*, 1282–1288.
30 D. Kamely, 'Military applications of biotechnology,' *Biotechnology* (1989) *7*, 447–451.

DNA transfer between procaryotes, bacteria and eucaryotes, but, it was recently found that DNA can be transferred between bacteria and yeast which is a eucaryote.[31] There are several plant species which can be traced to the natural cross-species pollination of other plants.[32] So it follows that genetically modified organisms (GMOs) are not significantly different from the organisms that could arise by normal genetic exchange, it just increases the rate of genetic reorganisation.

The Limits of Using Animals

People are more concerned about the alteration of animals, because they are sentient beings. There are major changes possible in animal characteristics and even category. We have seen the animals that we have made by conventional animal breeding, illustrated dramatically with the variety of dogs we now have. Nature itself is full of variety, and the selection of different characteristics in domestic animals has relied on this variety. But there is a point beyond which it is unethical to use animals as a means to our ends. There are similar problems to those existing for vivisection. There is room for government legislation to supplement the regulations based on avoidance of pain and endangered species, as there are other factors which are important. Public attitudes are becoming important as seen in the protest groups that have influenced decisions already. The boundary to the genetic manipulations we use on animals is going to be difficult to decide.

The Bible often mentions animals, as Israel was an agricultural community. God owns everything of creation, including all our cattle (Ps. 50:10) and He cares for them all (Gen. 8:17, 9:4, 10; Ex. 23:5; Deut. 12:23, 25:4; Num. 22:32; Prov. 12:10; Ps. 36:7, 104:10–11, 145:9, 15–16, 147:9; Job 38:26–27, 41; Jonah 4:11). God is not even careless of birds (Matt. 6:25, 10:29). God's mercies are over all His works (Ps. 145:9), and animals should also rest on the sabbath (Ex. 23:12; Deut. 5:14), and should be fed first, before the farmer (Deut. 11:15; Num. 20:8). Animals, however, can be eaten and farmed (Gen. 9:3; Deut. 12:20).

That is the issue on a broad scope, but what about the individual animals that are being made for such testing or use in general? In the case of clones, they are the same as normal animals. In the case of deliberately diseased animals, such as those that develop cancer very easily, or have physical abnormalities bred into them, the question is whether the means justifies the ends—not only in the actual use of animals, but in their creation that way at all, bringing them into life. There are those that develop cancer, such as the so-called 'Oncomouse' that was patented, and numerous other types of genetically modified animal strains, many in mice. Some of these animals are made so as to study the genes involved in

31 J. A. Heinemann & G. F. Sprague, 'Bacterial conjugative plasmids mobilise DNA transfer between bacteria and yeast,' *Nature* (1989) 340, 205–209.
32 S. Young, 'Wayward genes play the field,' *New Scientist* (9th Sept. 1989), 49–53.

development, including what are unique models for cancer research, as well as other worthy medical goals.[33] Embryonic stem cells are used to make some of these genetic modifications and new strains, and there is much research into the genes that control the developmental process. The ES cell lines make it easier to control specific genes, and also to generate many novel mutants.

What is surely an evil is the production of unnecessary pain in other beings. However, if we reduce our argument against using animals to that of the evils of causing pain, it would not restrict the use of nonsentient or painless animals.[34] It is possible to genetically engineer them to be painless, though I do not know of any examples of this having been done yet. While actively producing pain is seen as an evil, the sensation of pain is necessary as pain is important in the proper functioning of nervous systems, so feeling pain should not be seen as evil. We could imagine beings that could be made with limited sentience, only having the perception needed for basic survival, such as for limited self interest for eating, grooming or avoiding injury. In the extreme case we could consider animals made that enjoy being kept in factory style farms, or that want to be eaten, or are even masochistic. If we object to these experiments, we would probably be forced away from arguments based on pain, or preference utilitarism, in which sentience, the capacity of a subject for sensation, is the preeminent quality on which attitudes towards the treatment of that being by others is based. To a Christian the answer would be that it is because it is against the responsibility that God gave to man in looking after animals. It is not respecting other creatures in God's creation and is a misuse of power.

Transgenic studies after incorporating growth hormone genes into pigs and sheep have not shown any relation between gene number and expression of genes and growth rate. In fact many of the pigs died within 90 days of birth in the preliminary experiments, with significant problems of lethargy, muscle weakness, uncoordination, and susceptability to stress. Most of the transgenic animals did have improved weight gain (about 10%), but also had gastric ulcers, dermatitis, nephritis and other major problems.[35] This does illustrate the problems, and until these factors can be removed, even if it was economic to use these animals, it would not be ethical if they are going to suffer to that degree.

There will be major problems in agricultural and industrial use of new animals. These problems are not new in themselves, but the rapidity of change and the types of changes that are possible make it essential to look

33 C. Cohen, 'The case for the use of animals in biomedical research,' *New England Journal of Medicine* (198■) 315, 865–870; Council on Scientific Affairs, American Medical Association, 'Animals in Research,' *Journal of the American Medical Association* (1989) 261, 3602–3606.
34 D. Macer, 'Uncertainties about "painless" animals,' *Bioethics* (1989) 3, 226–235.
35 Pursel *et al.* (note 29).

at the possibilities. It will never be sufficient to justify animal use on the sole grounds of the ultimate benefit to man.

The humane treatment of animals requires at least that we seek to use the procedure involving least suffering. Alternatives involve reducing the number and refinement of procedures so there is less suffering, or replacement of animals by such methods as *in vitro* experiments, using cell lines, or embryos of lower status or larvae, or isolated organs, and computer simulation.[36] Government regulations that require animal testing of new drugs and compounds need to move with the development of alternatives, as they began to with the European Commission's decision in late 1989 to avoid the need for the LD50 test which killed many animals. Genetic techniques and embryo manipulation will reduce the number of animals used in vivisection because cloned animals can be used.

Environmental Release of Genetically-modified Organisms

The question of environmental release of GMOs is applicable to the release of bacteria, plants, animals and humans. The possibility of a novel and harmful virus being released and damage or disruption of the ecosystem are the main fears. In view of the potentially dramatic consequences, this is very serious. To be of a major practical use to worldwide agriculture, any GMO must be released into the environment. Only small scale agriculture can be conducted in closed environmental systems, though some important products used today are produced in that way, such as eggs from battery farming of chickens.

There have been many protests to prevent research, and they were delayed for several years.[37] It is generally difficult to make predictions about the potential of a given organism to become established and to maintain high populations in a given environment. The data obtained so far suggest that there is an extremely small likelihood of any survival of genetically-modified bacterial strains outside the area of use.[38] In these experiments, previous laboratory studies of bacterial behaviour predicted the observed environmental behaviour. Many pathogenic bacteria are continuously released into the environment in sewage, and millions of hectares of land are inoculated with *Rhizobium* each year to improve the growth of leguminous crops.[39]

A procedure for estimating the risks of each organism has been devel-

36 A. M. Goldberg & J. M. Frazier, 'Alternatives to animals in toxicity testing,' *Scientific American* (August 1989) *261*, 16–22.
37 P. R. Wheale & R. M. McNally, *Genetic Engineering: Catastrophe or Utopia*, Harvester, London (1988); OTA (note 14).
38 T. Suslow, 'Ice nucleation and the deliberate release of genetically engineered microorganisms,' *Trends in Biochemical Sciences* (1989), *14*, 180.
39 M. Sussman, *et al.*, eds., *The Release of Genetically-engineered Microorganisms* Academic Press, London (1988).

oped by the Royal Commission on Environmental Pollution.[40] They argue that because of ignorance we should not immediately categorise any type of release as sufficiently free of risk not to require individual scrutiny by the Committee. Each stage of the experiment should be subject to approval and licensing. It points out that the biggest brake on the acceleration of the number of releases would be any case of serious damage caused by slack regulations. This justifies close examination of each case. In Europe the regulations between countries differ, experiments are underway without any control in some countries, like Italy, but had been banned completely in West Germany. There have been several German biotechnology companies that have decided to build new laboratories outside of Germany to avoid prohibitive local regulations, such as BASF and Bayer.[41] Public opposition in Germany has even prevented the construction of factories which would use contained GMOs to produce medical proteins. In mid 1989 Denmark announced that they had authorised the first field trial of transgenic plants. The plants will be sugarbeet with either resistance to the herbicide Roundup, or resistance to a viral disease, rhizomania.[42] In the USA the Environmental Protection Agency has drafted new regulations in mid 1989 which do not distinguish whether the new organism is genetically modified but focus on the properties of any organism. In Japan there are experiments underway, and they seem to be adopting U.S. policies.

Most planned introductions are likely to be agricultural, so the negative consequences probably would involve an agricultural problem. Experiences with past introductions of organisms into new environments provides some clues as to the nature of the possible disruptions, though a better analogy for planned introductions of genetically engineered organisms is that with new crops or cultivars that have been introduced in agriculture in the past. There are some examples in nature where the acquisition of a single gene can cause ecological problems, such as antibiotic resistance genes that have been acquired by many bacteria. In the case of bacteria designed to degrade environmental pollutants, even if the degradatory gene(s) are transferred to other bacteria the effect would be beneficial. There have been some studies of bacterial colonies in polluted sludge/mud which have followed the fate of the novel genes, and have suggested only beneficial affects.

Overall these new genetic technologies promise much to aid world agricultural techniques. They are cheaper and should help to solve the pollution problems caused by the current fertilisers, herbicides and insecticides. If plants were made to use fertiliser more efficiently it would mean less fertiliser would run off into rivers causing pollution, and if they were

40 Royal Commission on Environmental Pollution, thirteenth report, *The Release of Genetically Engineered Organisms to the Environment*, London: H.M.S.O. (July 1989).
41 D. Dickson, 'German biotech companies flee regulatory climate,' *Science* (1989) 244, 1251–1252.
42 P. Newark, 'Danish lae to be less rigid,' *Nature* (1989) 339, 653.

made disease resistant then less problems would arise from the poisoning of the environment by chemicals. When preliminary trials in contained, controlled environmental situations have been completed for genetically modified organisms, and they are considered safe in the open environment by the controlling committees, those organisms should be able to be used in open environments.

One test case was the application by Monsanto Agricultural Products Company to field-test a soil bacterium (*Pseudomonas fluorescans*) which has been engineered to produce a naturally occurring pesticide (the toxin of *Bacillus thringiensis*) for the protection of the roots of crop plants.[43] Traditional chemicals are toxic to many life forms, but this pesticide is only toxic to a specific soil larva. This pesticide provides a better targeted and safer way to control insect pests.

One alternative to the release of live genetically engineered bacteria is to use dead bacteria. The U.S. company Mycogen received U.S. patents in 1987 for the invention of a process that kills bacteria while preserving their cell wall as a gelatin-like capsule which remains intact until the insect pests eat them, only then releasing the contexts such as a pesticide. These are alternatives to chemical pesticides, which are very damaging to the environment. The dead bacteria began field tests in 1987. The first large scale field tests of this pesticide (called 'Myogen Vegetable Product') have recently been approved.[44] Live bacteria will be more useful on fast growing plants such as lettuce, as bacteria will grow with the plant avoiding the need for reapplication. The capsules are better for transporting, and have a higher concentration of toxin than bacteria, compared to bacteria which have to grow in the open environment.

The World's first commercial pesticide based on a live genetically engineered organism went on sale in Australia in March 1989. It is called 'NoGall', and it protects stone fruits, nuts and roses from a disease called Crown Gall disease, which causes worldwide annual loses of at least US$150 million.[45] The 'pesticide' consists of a harmless strain of the disease causing bacteria, that will live on the same leaves, and produce an antibiotic which kills the disease-causing strain.

ES cell lines make the creation of transgenic animals easier, and give much more control over the exact genetic change transferred to the animals. If we are concerned about the targetting of gene changes then they may have definite advantages. The genes can be manipulated in their natural chromosomal environments, whereas the use of conventional methods for introducing DNA sequences into the germ line allows little

43 OTA (note 14).
44 S. Watts, 'Dead microbes sidestep rules on genetic release,' *New Scientist* (Oct. 1989), 21.
45 B. Wright, 'Gene-spliced pesticide uncorked in Australia,' *New Scientist* (4 March 1989), 23.

control over the chromosomal site of integration and the number of integrated copies.

At recent conferences on GMOs the concern has been switching somewhat from the environmental issues to the issue of safety of the end product for human consumption. There are worries about the genetically engineered crops, and many will soon be under scrutiny in the USA for Food and Drug Administration safety. There are concerns that there could be harm from high levels of some toxins, which are probably of low risk. There was, however, the case in the 1960s of a new strain of potato called 'lenape' which had high levels of a usually trace level toxin, and caused illness after eating. There are also unknown affects on allergies of people. The concerns also cover grains or food that can be given to animals as feed.[46] It has been found that some plant defenses against pesticides involve the synthesis of carcinogens.

The Way Forward

In this study some ethical issues raised by the application of newly developed genetic techniques have been considered. We do not need to move to very novel ethical theories to consider the implications of new genetic technologies as some propose.[47] Rather, these new problems reflect similar issues to those of existing and older problems. The problems of GMOs come down to two major issues; Stewardship (including cruelty) and the free environmental release of GMOs with the possible ecological dangers.

The insertion of new genes into animals should continue where necessary for the study of biology when there is no clear detrimental affect upon the mutant animals. There is a balance in each case between the importance and effect of an experiment and the status of the animal. Where there is likely agricultural benefit without major suffering or change then new genes should be able to be inserted. In agriculture there are definite advantages in the use of some artificial reproduction, embryo transfer, and clonal reproduction, that do not raise unsolvable ethical dilemmas. Some genes may be found which it would seem wrong to insert into animals, such as genes which control basic animal behaviour, or pain sensitivity, or introduce disease or excessive suffering to them. In medical research using clonal animals, there are problems similar to those existing for vivisection, with the need perhaps to develop criteria for judgement less based on pain as argued above. We may need to consider the protection of species integrity or bodily form, which have been neglected in recent ethics. We may also need to work towards promotion of a higher view of nature, which

46 I. Wickelgren, 'Please pass the genes,' *Science News* (19th Aug. 1989), *136*, 120–124.
47 D. Suzuki & P. Knudtson, *Genethics: The Clash Between the New Genetics and Human Values*, Harvard University Press, Boston (1989).

would condemn the misuse or abuse of nature not only because it is wrong but because of the bad effect on human values.

Some of these techniques do raise different and much more complex problems when applied to human beings. We may not object to altering the sex-ratio of agricultural animals, or even of endangered animals in the wild to improve their chances of species survival, but we may oppose sex selection in humans. We can not argue that because a technique is unethical for human use it should be banned in animals, as shown by currently accepted practises. We can draw the line between animals and humans.

There will be novel situations that will make us think more about our use of nature, and particularly animals. This is good if it makes us rethink our attitudes, and perhaps question some accepted practises. We will have many new possibilities in the decade ahead. Within ten to fifteen years we will have the sequences of all human genes, raising the question of future animal research which may transfer specifically human characteristics to animals. There are potential advantages for both medicine and animal welfare, but we do need to reexamine where the ethical limits are. It is important for Christians to be involved in deciding the future scope of the use of these techniques. We need to examine what type of society we are making for ourselves, and we as Christians should be moulders, not the moulded. It must be clear to all of us that science will not solve our social problems, but it is an important part of our management of the earth.

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