that these elements had more meaning than the concepts of 'full disclosure', 'competence' and 'fully autonomous choice'.

Clinical freedoms and innovation were the subject of some vigorous discussion. In the context of rationing, there was some division of feeling about the conflicting needs to collaborate with management and the duty to continue to act as advocates for patients. The conflict between economic exigency and best practice remains unresolved, but there was general agreement that this conflict is now a real part of every day practice, and that the moral issues are still not fully defined.

It was interesting to note that throughout the workshop, the participants had used three different structures for examining ethical problems – principle-based ethics, virtue ethics and rights and duties. This was perhaps not made quite explicit, and some formal presentation of structures that can be used for ethical thinking might well be incorporated in future workshops of this kind.

In summary, this excellent workshop achieved several things. It made surgeons more aware of the essentially aporetic nature of moral thinking, and of the complex interrelationships it has with the law. It emphasised strongly how important ethical thinking will become, as economic stringencies increasingly influence medical practice. It delineated some of the matters peculiar to the discipline of surgery, and reinforced the College's wisdom in entering the ethical field so publicly. The workshop concluded with the hope that the College would continue to expand its ethical activities and its liaison with the various centres for ethics and bioethics.

Dr Hall and her colleagues deserve our thanks for both the excellence of the organisation of the meeting and its content.

Article

The Cloning of Dolly: Heralding the New Future of Biology?

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The creation of Dolly, the sheep cloned from the mammary cells of her 'mother', as heralded much international interest. But what is cloning, and why has it generated so much interest? The terminology was first coined at the beginning of this century, and the technique itself, at least in horticulture, has been with us for a long time. Its botanical use refers to the propagation of plants carried out by using grafts, cuttings and bulbs, and more recently tissue cultures etc. For instance, advances in the technology of radiata pine propagation are enabling the development of clonal forestry in New Zealand. But its wider use in biology refers to the asexual reproduction of organisms that normally reproduce sexually.

What this means is that the genes or DNA from one organism are copied and a new organism – a genetic replica – created from it. Like many things in science that grab the public imagination, cloning is not new. In 1952 researchers took an embryo from a frog and cloned it creating an exact copy of the original frog. In the 1980s they took a red blood cell from a frog, copied the DNA and created tadpoles. However, these tadpoles died at about the time they would have been expected to develop into adult frogs. Similarly, in 1996 researchers in Scotland reported that they had cloned sheep from an embryo cell line. This has been repeated for the second time only in New Zealand this year by the Molecular Embryology staff at AgResearch Ruakura. This year the Scottish group of researchers reported that they had cloned Dolly, from the DNA contained in the mammary cells of Dolly's 'mother'. Human embryos were also apparently cloned in 1993. They were provided by an infertility clinic and were defective and due to be discarded. The cells of the embryos were separated and a few individual cells developed into 32-cell embryos.

Identical twins are in a sense clones, since they share the same genetic material. Identical twins may in fact resemble each other more closely than clones since, unlike Dolly and her 'mother', identical twins develop from eggs with similar cytoplasmic constituents, they share the same uterine environment and they may share similar environments after birth. In contrast, Dolly and her 'mother' developed in separate breeds of sheep and grew up in a research environment some six years apart.

Forms of embryo cloning

The cells of the early embryo are considered to be undifferentiated. This means any cell has the potential to grow into a bone cell, or a brain cell, or a liver cell, etc. However, once differentiated, it's generally accepted that a bone cell cannot grow into a liver cell, nor can a brain cell grow into an ear cell. It is this feature which gives rise to the different forms of cloning. In embryonic cloning, the undifferentiated embryo can either be bisected to form two identical embryos or the cells can be separated and individual or small groups of cells, allowed to multiply, growing into many copies.

Alternatively, the technique of nuclear transfer can be used. Here, the nucleus of each of the cells, containing exact replicas of the DNA or genetic material of the original embryo, say a sheep embryo, is then transferred into surrogate unfertilised egg cells from which the nucleus has been removed (while the recipient egg is enucleated, the mitochondria in the cytoplasm still contains their own DNA). These are fused and activated by a small pulse of electricity and then grown and implanted into foster sheep, resulting

eventually in the birth of a number of identical or cloned sheep.

Last year the researchers in Scotland did something unique. They produced Morag and Megan by nuclear transfer, using early differentiated cells which had developed from cultured sheep embryo cells. This has been repeated this year at Ruakura with the birth of Thomas and James – clones from an embryo cell line which had been cultured for about two months. This year however, the Scottish group took this procedure one step further. Instead of using the early differentiated cell of a sheep embryo, they took a differentiated somatic cell from a mammary gland culture and produced a cloned embryo which, as before, was allowed to develop and then implanted into a surrogate ewe which eventually gave birth to Dolly. The Scottish workers have therefore done what was thought impossible – undoing the process of differentiation. This is achieved through starving the cells of nutrients so their active genes switch off. As before, Dolly has the same genetic makeup as her 'mother's' mammary cell; she was named after Dolly Parton. The significance of this feat is apparent when you consider that it will be possible to clone animals of known value producing many genetically identical individuals. Possibilities include animals with outstanding genetic characteristics (e.g. lean meat) or the sheep genetically engineered by the same Scottish researchers, to produce the human pharmaceutical alpha-1-antitrypsin in their milk in order to treat cystic fibrosis and emphysema, or even a highly successful racehorse with a record of winning the Melbourne Cup. In contrast, when an embryo is cloned, although it may have a fine pedigree, it has no track record and the clones may not perform as well as anticipated.

What are the issues?

First, one of the benefits mentioned above is the *multiplication of animals with desirable traits*. Particular animals that are extremely rare can be multiplied so that we can quickly gain a reasonable population. As well as applications in the conservation of endangered species, this might also be applied to animals which have been genetically engineered, since the present success rate of genetic engineering is low and cloning could allow their rapid multiplication. In a similar way, valuable farm animals such as those demonstrating extraordinary resistance to parasites could be rapidly multiplied. Theoretically, the technique of cloning is potentially faster and more accurate than more traditional means of increasing numbers, such as superovulation, artificial insemination and embryo transfer. It could lead to large one-off increases in genetic gain equivalent to many years of traditional breeding. It could also allow animals to be selected for characteristics which can only be measured after slaughter – one clone is slaughtered and if the desired characteristic (e.g. some aspect of meat quality) is present, the remaining clones can be introduced into the farming industry

Secondly, there is the issue of the *health and well-being of animals* produced using these techniques. It is early in the development of the technology, but there have been reports of problems. For example, in one study of cloning in dairy cattle 60 to 70 per cent of calves were born completely normal, but a further 20 to 30 per cent were larger than normal at birth (up to twice the normal size) despite having a normal gestation. These required caesarean births. However, most calves survived and developed into normal animals within a few months. The final 10 per cent of calves had other abnormalities including joint problems. Some of the cloned sheep also appear to have suffered side-effects, with lambs dying during pregnancy and around birth due to congenital abnormalities, and again some born larger than normal. One objective of the cloning research is to overcome these problems by developing the technology to a stage where the offspring are as healthy as non-cloned animals, if not those animals susceptible to such problems can be avoided. In any event, it is suggested that the principle of conservation of welfare is used – the animals should be no worse off for having been cloned. Another measure of well-being is life expectancy and there is a question regarding the age of the cloned animal. Dolly was cloned from a six-year-old sheep. Since genes and DNA tend to age along with the animal, does that make her six years old at the time of her birth? One scenario might be that Dolly will die six years earlier than normal. This would not appear to be a problem to farmed animals, since most fail to realise their natural life span. However, a clone taken from Dolly when she is six years old, in other words a clone of a clone, may have DNA that is twelve years old at the time of birth. Now the natural life span of a sheep is something around twenty years so, that if the DNA ages the making of clones from clones may have a limited potential.

The third issue is that of *animal integrity*. Is cloning somehow interfering with, preserving or even enhancing the integrity of the animal and therefore somehow inherently right or wrong? Integrity has been variously described as the intrinsic value, naturality or intactness of the animal or its genetic material. Obviously more traditional animal-breeding techniques, and even the cloning of plants, may also affect integrity – a subject of much philosophic discussion.

The fourth issue is that of *genetic uniformity*. Cloning large numbers of a few valuable individuals will result in an increase in the number of genetically uniform animals within a population, reducing overall genetic diversity. If these animals prove to be genetically susceptible to a disease, obviously the whole population of clones will be similarly susceptible and this risk needs to be established. However, while the technology has been portrayed with the expectation that large numbers of clones will shortly be farmed, the reality is that the technology is very inefficient and is not yet commercially viable – except possibly for the multiplication of genetically engineered animals. In any event, this problem is not specific to cloning. Perhaps the most famous example of the problems resulting from genetic uniformity is the Irish potato famine, but modern equivalents exist.

The fifth issue is the possibility of *social and environmental changes* relating to the widespread use of this technology. For instance, will it increase our dependency on biotechnology companies, and will this be an advantage or a disadvantage for farmers, consumers and others? What environmental changes might be expected from the cloning of highly productive dairy cows resulting in, say, fewer but larger farms producing our dairy products? Conversely, there may be increased numbers of small herds producing niche products.

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Island, or Charisma? In all likelihood we will end up doing all three, in some form or another. But on balance I think we are unwise. We would be better to find alternative ways of producing eggs, to experience the grief that we have wiped out yet another species (and then allow our grief to motivate us to look after the world's ecosystems), and to accept that it is no great disaster that equestrian eventing still combines a combination of training, skill, *and* breeding.

Information for Contributors

The *Otago Bioethics Report* publishes short papers on Bioethics, particularly those with an emphasis upon current New Zealand issues.

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The final issue concerns the *implications for humanity* – the cultural ideal we want for ourselves. This issue relates to the sort of people we want to become – people who regard the non-human world as a means to an end, or people who respect the non-human world for its own sake. It is this aspect which has captured much of the public and media attention. Someone who sees nature as a resource to be used might defend cloning, whereas someone who considers all life forms sacrosanct might not. Many of us take the middle ground, accepting that while nature is a source of raw materials, it is also something to be used wisely and with care. Similarly, we accept that there needs to be a balance between human and animal needs, and that animals may be used but only if that use is humane.

It is well to remember that cloning in animals might well have some positive spin-offs for humans; for instance, cloning animals may produce humans health products or products which allow improved goods to be produced. Also, developing the technology in animals may help develop human cloning for assisted reproduction and organ transplantation programmes. However, human cloning raises ethical issues beyond the scope of this paper.

Undoubtedly, the most well-known implication, if not fear, for humans is that which we normally associate with Hitler and *The Boys from Brazil* – the multiplication of undesirable so-called 'elite' individuals. This aspect has gained most recent attention, leading one critic to comment '*The real sheep are the media who have blindly followed the cloning story, shrieking of its horrors.*' The newspaper reports of the cloning of Megan and Morag last year, included headlines such as '*scientists welcome move to clone sheep*' and that it may '*herald a brave new farm world*'. However, the newspapers also picked up on something which was not presented in the original science article, that some animals suffered serious defects. In contrast, this year's report of the cloning of Dolly resulted not only in headlines such as '*science of the lambs*' and '*clone on the range*' but more significantly that such technology '*raises alarm over humans*', and '*Frankenstein fear revived*'. Thus, at present, we appear to be debating the morality of cloning of animals on human grounds. Is this sensible for the future of both animals and humans? It is accepted that animals and humans can be treated differently (for example, moribund animals must, by law, be euthanased). It would be a pity if the benefits of animal cloning were not fully realised, because of the perceived harms of human cloning.

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