POLLY, DOLLY, MEGAN, AND MORAG: A VIEW FROM EDINBURGH ON CLONING AND GENETIC ENGINEERING

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INTRODUCTION: ETHICS IN A MEDIA CIRCUS

On February 23, 1997, news of the first cloned mammal to be produced from somatic tissue made Dolly the cloned sheep an overnight global media sensation, and made the Roslin Institute's team leader, Dr. Ian Wilmut, world famous. When I had asked Ian some three years before to take part in a working group on the ethics of non-human genetic engineering for the Church of Scotland, neither of us had any inkling of how these questions would be thrust into the spotlight of the world's media. The scale of the reaction was beyond any foreseeing.

It has become possibly the most hyped ethical issue on technology yet to emerge, but it is doubtful that the saturation coverage has led to a comparable degree of understanding of the issues which Dolly raises. The competitive scramble of newspapers and magazines to cover the event and its implications led to a strange mixture of science fact and fiction, sometimes inextricably entwined. Every bizarre possibility for human clones was explored irrespective of any factual basis, and such cloning was seen as inevitable regardless of the numerous barriers in between. While it seems that just about everybody in western culture has heard about Dolly, rather less have an accurate conception of what is and is not going on. The instant nature of media reporting is not conducive to careful ethical reflection on novel and complex issues.

Cloning became as much a media circus show as it was a piece of science and an ethical challenge. It remains to be seen whether the science or the circus will have the greater long term impact. For the time being, in examining cloning issues, we have to examine the hybrid of the ethics of a science so new that its ink is still wet on the page, with public perceptions in the age of the Internet, and sound byte ethical judgments motivated primarily by the demands of sub-editors

for catchy headlines.

It was partly to avoid this knee-jerk ethics that in 1970 the Church of Scotland set up the Society Religion and Technology Project. Ever since it has been attempting to cast an informed eye on a wide range of technological issues, by engaging directly with key scientists involved. So it was that at the end of 1993 we set up our working group of experts which has brought together geneticists with specialists in ethics, theology, sociology, risk, agriculture, and animal welfare. This paper, while not a product of the group directly, nonetheless draws from many of its insights.

TECHNOLOGY AND IMAGINATION

For most Christians, to do technology is to do something God-given. It is inherent in our nature to find ways to shape the created order around us. When the ancient Genesis account speaks of humans bearing the image of God and naming the animals, something creative is implied. It is not just that we want to classify. We imagine beyond mere description, and in imagining we conceive new things, things that have not been before. Technology is the rather odd word we use that extends beyond knowledge and sees application also—not only to call a particular woolly mammal "sheep" but to see what sheep could mean to humankind.

It is a very long step, however, from saying "sheep" to imagining the asexual genetic replication of human beings. One feature of the media coverage was overwhelming emphasis on this aspect, with an immediate jump to assuming it was nigh reality already, or a resignation that someone will do it in a private clinic somewhere safe from regulations. One of the most striking features has been the almost absolute belief that science can and will leap any barriers, both among the fearful of what it will produce, and among those who can hardly wait. Certainly Dolly represents a classic example of something thought impossible, but there is an unwillingness to acknowledge the parallel reality that science just as often gets stuck. After the first flush of the press conference on the initial discovery, the reality is often quite a lot less ambitious. We believe what we want to believe about science, it seems.

The other implication of this skew in the coverage is that the ethical issues

surrounding the fact that we can already clone animals were given comparatively short shrift. This paper hopes, in passing, to redress the balance a little.

"HUMAN CLONING IS WRONG"; ON WHAT BASIS?

Perhaps the most striking feature of the immediate and continuing public reaction in Scotland and the United Kingdom as a whole and across Europe has been the widespread intuition that cloning is inherently wrong. This was coupled with a mixture of relief that at least UK law—the Human Fertilisation and Embryology Act 1990—already prohibits human cloning by embryo splitting, and could be amended relatively easily to outlaw the nuclear transfer route, and concern that other legislation, notably in the USA, would be too lax to prevent it happening. There have been other voices, which will be considered later, but first I want to examine on what these dominant intuitions are actually based. It turns out to be surprisingly difficult.

There are four main components: (1) that it is unnatural to clone, or otherwise (2, 3) offends intrinsic principles; (4) that it would be unacceptably manipulative of human beings and would set a socially dangerous precedent.

Some would extend this also to animals, saying (5) that it is an unacceptable intervention into the natural processes of animal reproduction. (Others would draw a distinction and would not see a fundamental objection to animal cloning.)

One cannot escape in these reactions some shaping by the social context into which the announcement was received, and its reinforcement by certain associations which were made repeatedly in the media coverage. Prominent among these were the notion of human genetic improvement by germline therapy, the eugenic programmes practiced not only by the Nazis but by several nations normally held as scions of democracy, like the USA and Sweden, as well as ideas of armies of soulless humanoids and other imaginings engendered by a whole corpus of science fiction—notably Huxley's *Brave New World* and that evidently less literary achievement, *The Boys from Brazil*. These associations contributed to the tendency to muddle cloning with genetic engineering and unrelated inventions like the notorious mouse with a human ear on its back. Here was the nadir of human over-intervention in nature, which, like BSE, will surely see nature turn

round and strike back at us for our presumption.

1. UNNATURALNESS?

Arguments for unnaturalness are of course questionable in ethics, when so little remains around us that one might with any justification call natural, and when nature itself is a constantly moving target. It is so much a social construct that some dismiss it altogether. But in our Edinburgh genetic engineering study we came to the conclusion, in the context of xenotransplantation, that we should not throw the baby out with the bathwater. It seemed to us, as to others before us, that even if it makes little use as an absolute philosophical concept, there is something important in the concept, "unnatural," which those of a more reductionist or scientifically optimistic bent ignore at their peril. This is the perception that there are scientific ideas and technological interventions that are now going too far to remain in tune with what we perceive "natural" to mean, notwithstanding how far we have intervened in nature to date. Despite how relative our ideas of "natural" are, it is a valid idea and it tells us something.

Take the idea that we might have infertile couples enjoying the experience of bearing children by cloning one member of the couple. We do not know if this would be possible, but suppose we could. For many people, to do so would be too far removed from the idea of what is appropriate to the way things are. For others, it is unfamiliar, but like heart transplants, it is something we will get used to. We will return to these points at the end.

Of course, the argument that cloning is absolutely unnatural falls simply because, for example, in the plant kingdom cloning is a fairly common phenomenon. If you bury a potato in the ground, it clones itself. There are also some animal examples, but not, significantly, in mammals or humans. There is a biological distinction. And this raises a most pertinent question. Should we respect this biological distinction, or should we celebrate our human capacity to override such limitations? Since we do have the capacity to alter what we regard as natural, the argument that cloning is unnatural switches to one of what we change. Need we respect any biological distinction? I want to suggest a number of grounds why we should not normally press the human override button on either animal or human cloning.

2. DIVERSITY

In intrinsic ethical principles, more substantial ground is found in the question of the diversity of the natural order, and in genetic diversity in particular. Humans and sheep use sex to reproduce. Basic evolutionary genetics has certain rules. For a species to survive and flourish by sexual reproduction requires the species to maintain a certain level of genetic diversity. Since in selective animal breeding there are well recognized limits to in-breeding before serious problems arise, how much more so is this a problem if one was to clone. These limits reflect something about the nature of things. This seems to illustrate a fundamental principle, for which Christian theology provides some important insights.

For the biblical writers, one of the most characteristic features of God's creation is its variety. Throughout the Bible, in commandments and stories and poetry, there are repeated allusions to it, and some most striking pictures are painted of a creation whose sheer diversity is a cause of praise to its creator. On this basis, it is argued that to produce replica humans or animals on demand would be to go against something basic and God-given about the very nature of life. Indeed, where God evolves a system which works on principles of diversification, one might reflect how typically human it is to select out certain functions which we think are the best ones, and replicate them. Where God opens up boundless possibilities for the whole life of an animal, humans would reduce them to a narrow blueprint, for their functional value.

Cloning individual creatures could therefore be seen as a Babel image of misplaced control. There is a myopic tendency in what the biblical writers describe as our fallen human nature which sees ourselves only for what we can get out of each other, or control in each other. Reductionist science in particular tends to lead us to think in narrow, reduced confines about ourselves. God, in this view, conceives of us far more widely, as unique persons, who are complexes of innumerable functions, who build up relationships based on that diversity. Indeed, the freedom and diversity in people is one of the things we prize most about each other. Sex creates new possibilities in order to produce more varied life. Deliberate cloning, by contrast, is a centralized and even totalitarian approach, where the very aim is predictability, replication in order to exercise control over something.

In the limit this would suggest that cloning is absolutely wrong, no matter what it was being used for. This intuition runs deep in many people I have spoken to in the recent past, both inside and outside the church. I will argue that there are circumstances where scale and intention might lead to a modification of this basic thesis.

3. TWINNING AND CLONING: RANDOMNESS AND INTENTION

First we must consider the case of twinning. If cloning was absolutely wrong, some have argued, why then do we have twinning? Identical twins are natural clones, who are much more identical than anything which Roslin's nuclear transfer technique could produce. Genetically, the mitochondria in the outer part of Dolly's cells come from a different individual than the DNA in the nucleus. And the nurture is entirely different—a different womb, in a different family setting, and at a different time. So if we say no to cloning, are we then saying that twins are abnormal?

Biologically, in one sense, human twins are not the norm, but the unusual manner of their creation does not make them any less human. We recognize that each is a uniquely valuable individual. Similarly, it is important to stress that cloned humans would not be subhuman androids with human bodies but no souls—unless sexual reproduction were associated per se with ensoulment, which most Christians would not agree with. Unlike twins, however, clones would lack certain conceptual parts of our notion of humanness. They would not have both a direct biological mother and father. Their genetic composition would not be a chance, indeterminate event, but would be pre-programmed. That is not the case with twins. On this basis, the analogy with twinning is not an adequate justification for cloning. Twinning is a random, unpredictable event. Cloning is intentional, controlled action to produce a specific known end. Their intentions belong to very different ethical categories. This leads us to the main consequential objection to human cloning—instrumentality.

4. INSTRUMENTALITY

From a consequential viewpoint, four questions arise: intention, identity, relationship, and scale. There is a basic principle, that to replicate any human being technologically is a fundamentally instrumental act towards two unique

individuals—the one from whom the clone is taken and the clone itself. In the rash of speculation on bizarre applications for cloning a full human being, almost all displayed this attitude.

Examples ranged from:

—the ridiculous: mad dictators creating armies of themselves;

—through the pathetic: cloning a dying child or parent to help those bereaved cope with the loss;

—to the serious: cloning an infant with a predisposition to leukemia as a source of bone marrow which would suffer less tissue rejection problems.

In each of these cases the clone would be a means towards someone else's end, created for the primary benefit not of the individuals themselves but of some third party. To create another human being other than primarily for their own sake raises a serious objection, as a removal of the ontological freedom of that new person. It also implies a potential for human exploitation of the cloned and the clone. This would represent an abuse of human dignity, which would in the view of the Church of Scotland General Assembly (forthcoming) justify banning worldwide the cloning of a human being.

Psychological Effects; Identity and Relationship:

No one knows what would be the psychological problems of identity arising from nuclear transfer cloning. Am I just a copy of someone else who already exists and not really "me"? Am I really someone else but put into a different womb? What will be my relationship to the one I was cloned from? Instead of being the unique genetic product of both parents, I am the copy of one of them. No one can predict what the response would be. Presumably they would vary from person to person. I suggest there are sufficient dangers so that the precautionary principle should apply. In other words, even though one could not be sure how many people would suffer in this way, it would be wrong knowingly to inflict that risk on someone.

Other Consequential Objections:

There are also sufficient unknowns about physical problems in pregnancy with cloned sheep and cattle to suggest that human cloning experiments would violate normal medical practice. There are also unknown factors of aging. How old is Dolly? Is it her age since her birth, or her age since birth plus the age of the tissue from which she was taken? No one knows what the effect is of nuclear transfer on aging processes.

5. ANIMAL INSTRUMENTALITY

I said at the beginning there had been excessive concern about humans that we may never be able to clone, and a neglect of the ethical issues about animals which we can already clone. One can see a distinction between animals and humans, both deontologically and in consequential terms. Issues of identity and relationship do not apply in the same way, but are more about what is the right treatment and welfare of animals. The question of intent is important, as is the matter of scale. Here I would draw a distinction between Roslin's work and some of the animal applications to which it might be put.

Small Scale Special Cloning:

Contrary to popular perception, Roslin's basic work on nuclear transfer is not primarily aimed at cloning, but at finding more precise ways to do their existing work on genetically modifying animals. In 1986, Roslin researchers made the ground-breaking discovery that it was possible by introducing one or two genes of human origin into sheep and other mammals to produce therapeutically useful proteins in their milk (James, 1993). This has since been developed by the Edinburgh company, PPL Therapeutics, and the leading protein alpha-1-anti-trypsin is undergoing clinical trials. This can help counteract the lung damage found in emphysema and cystic fibrosis.

Of all the examples of animal genetic engineering our working group looked at, this posed the least ethical concerns, since the intervention in the animal is very small for a considerable human benefit. Most of its concerns lie in the experimental stage, since genetic engineering in sheep is a very hit and miss process, performed by injecting into an early embryo, with about a 1% success rate. A lot of animals must be created to get one with the right gene in the right

place.

Roslin's aim is to do the modification in a cell culture, select the right one and then grow a full animal from the cells. This is possible with the embryonic stem cells of mice, but not in larger animals. The main aim of Roslin's nuclear transfer work was to provide a way around this, first with an unmodified sheep—Dolly—and then from genetically modified cells, which produced the genetically modified lamb, Polly, announced in July, 1997, with a human gene inserted. From the point of view of the original work, Polly is in a way a more important breakthrough than Dolly, because she proves a principle. If indeed this can be done with the precision and reproducibility which they hope for, it could transform farm animal genetic engineering, enabling more precise manipulation using many less animals, and also open a much wider range of genetic changes and applications.

The fact that Polly is a clone is actually a side effect of this, but one they would make use of to produce 5-10 founder transgenic animals; thereafter, these would be bred naturally. I would argue that in this example cloning is a kind of double effect. This is a very limited application, the point of scale to which I referred. Its main intention is not to clone as such, and there is apparently no natural way to the same end. It therefore lacks something of the instrumentality of other applications. I would argue this could be considered ethically permissible, even though I would say that cloning of animals is normally questionable.

Animal Welfare Issues:

We also need to be sure about the animal welfare aspects even of limited cloning. Questions have been raised about the number of failed pregnancies and unusually large progeny which appear to be resulting from Roslin's nuclear transfer experiments to date. While the suffering is not so great as to put a stop to this work, it is clearly necessary to understand the causes and establish whether the problems can be prevented, before the methods could be allowed for more general use. If after a reasonable time there seemed little prospect of doing so, however, one would doubt whether it was ethical to go any further. (This also points to the serious possibility that any attempt at human cloning could be extremely dangerous for both the clone and the mother, and thus medically

unethical, irrespective of wider ethical concerns.)

Routine Cloning for Animal Production:

If Roslin's main intention was not to clone, they have not been slow in pointing to ways in which cloning could be used in selective breeding, and their patent applies to all animals. The suggestion is to use Roslin's technique routinely to produce genetically identical copies of the best animals in a breeding programme. Here it seems to me we run into some much bigger ethical problems of inappropriate instrumentality. Cattle cloning by embryo splitting is already used to a limited degree, so what is the problem? It depends on one's background perception of what is permissible use of animals. There are wide differences, between American and European attitudes and amongst European countries. If animals are things we can put to good use, and you support a technological approach to agriculture, then why not clone your best breeding stock so that farmers can do a step jump in the genetic merit of their herds of cattle or pigs? Or why not produce reproducible cuts of known, high quality meat for the supermarket shelves, by cloning the animals you fatten for slaughter? If animals are God's creatures, not everything is permissible, and a recognition of their inherent worth is required of humans, and in particular a recognition of the distinction we make between what is alive and what is not.

I would suggest that cloning is the place where we should stop in our technological approach to animals. To clone routinely would apply a factory model of mass production too far into the realm of living creatures. We need to remind ourselves we are not dealing with identical widgets on a production line, but living creatures, useful to us, but still creatures. This is especially true if natural means exist, and the main gain is improved production efficiency for supermarkets. I would argue this was an inadequate justification for doing something which goes against normal principles of diversity. Routine animal cloning would take the mentality of commodification one step too far.

This might seem an over-reaction, if one could look at the track record of areas where a production orientation has been applied to animal breeding and point to our caring and responsible behavior towards animals. Sadly this is not the case, however. Poultry so overbred for meat production that there are severe welfare problems, and many other examples, do not inspire the confidence one

would need. In their report on xenotransplantation, the Nuffield Council on Bioethics (1996) observed that if the background was one of harmful treatment one should ask of any genetic technology whether it would make things worse or better. In the light of existing welfare abuses in farm animal breeding, a balance is needed, with greater restraint towards living creatures.

Possible Appropriate Uses of Animal Cloning:

There are some other uses which might be considered. Here one is in the realm of speculation again. If the survival of an endangered species was simply dependent on increasing numbers rapidly, as opposed to increasing genetic diversity, it might be an option. It might also be acceptable to clone animals in experiments to assess environmental impact in animal diseases. All of these could only be limited in scope, however, to avoid the diversity problem.

VIEWS IN FAVOR OF CLONING AND SUMMARY OF ETHICAL CONCERNS

This paper has so far argued that cloning represents: a reversal of the principle of diversity in mammals and humans; an instrumental use of humans; a psychological danger to the humans involved and their relationships; a physiological risk to both mother and embryo that would be unacceptable in medical ethics; a commodification of animals to an unacceptable degree if used in normal production; a method in which limited animal applications might be acceptable (notably Roslin's own work); but a technique with animal welfare problems that would need to be resolved.

In the main, this represents a fairly strong catalogue of objections. Not everyone agrees, however, and in particular, arguments have been advanced in favor of various limited forms of human cloning. This final section critiques some of these, and also some of the assumptions which seem to underlie more positive views towards human cloning.

Limited Positive Medical Uses Of Human Cloning

There has been wide speculation on possible uses for Roslin's nuclear transfer work, much of which is premature. Lord Winston, Steve Jones, and

Matt Ridley have, however, all pointed to what they see as the great promise for human medicine from the technique which Roslin has developed. In an editorial in the British Medical Journal, Lord Winston (1997) cited:

—research into aging, and cell development in relation to human development and disease;

—the possibility that if it is possible to reprogram an udder cell to be totipotent, it might also be possible to reprogram a particular cell to develop into some other body organ or tissue, which might be grown as a separate entity for transplantation; and

—further understanding of the causes of infertility and the development of new treatments.

Since all of these notions are at present largely speculative, it would be hard to advance a definite opinion on their ethical acceptability. It may be that some would not raise insuperable objections. In recognition of this, the Church of Scotland stopped short of calling for a blanket ban on all applications of cloning techniques (Supplementary Reports, 1997). It would equally be a mistake, however, to assume that these would necessarily be ethically acceptable because they did not involve cloning a full human being, or that human medical benefits constituted sufficient justification alone. Each would need careful consideration. Three examples serve to indicate some of the likely issues.

For an infertile couple to have a child by cloning one of them would not normally be thought of as an instrumental act, and might at first sight sound like a compassionate option to offer to childless couples. As observed above, however, there could be serious ethical problems, notwithstanding the anguish which childlessness brings to many couples. It would not be the biological child of both parents in the normal sense. For many this might be seen as taking the technological harnessing of the desire for a child one step too far, a means which is not justified by the end. Parenthood is not an absolute. In one Christian understanding, children are a gift, not a right which we can presume that God or life should give us on demand. As also discussed above, there would be serious physical risks in pregnancy which on the basis of the animal work would seem unacceptably high, and it would also raise profound and unpredictable questions

about the identity of the child, which would be a kind of twin of one of its parents. These risks present a strong case that this would be an irresponsible action to take.

The prospect of creating entirely separate organs for donation would raise profound problems about the nature of a human being. A reductionist and utilitarian view might see the creation of separate human parts as of no particular significance beyond the medical benefit that might accrue. A more holistic view of the human person might well find the idea repulsive. However, it may never get to that stage, because of the nature of the animal experimentation that would presumably be necessary enroute. In the face of such examples as the headless frog (*Sunday Times*, 19 October 1997), this application might not be as acceptable as first thought.

In the USA, President Clinton's special ethical commission (Bioethics Advisory Committee, 1997) concluded that it would be acceptable to produce cloned embryos for research provided they were destroyed after a certain stage of development. This seems an extraordinarily instrumental approach which would present serious ethical obstacles for many people who regard the early human embryo as more than just a ball of cells for experimentation. To produce a potential human in the knowledge that it would be ethically unacceptable to grow it to term should suggest it was inadmissible to create such an embryo in the first place.

To keep these notions in perspective, there are as yet only a few pieces of animal data, and certainly insufficient theoretical understanding of Roslin's method to provide a sound basis for proceeding. It remains to be seen how many speculative uses prove realistic, not least because of important differences in embryology among mammals. Nonetheless, the fact of Dolly is embodiment enough to begin to explore such ethical implications. While such questions are theoretical for the moment, it would be imprudent not to consider which options would or would not be ethical to pursue, rather than simply wait for another dramatic result to surprise us.

IS NOTHING SACRED? THE ILLUSION OF TECHNOLOGICAL INEVITABILITY

An underlying concern from all these speculations is an attitude of

technological inevitability on the part of those pressing for advances. Steve Jones in a recent radio programme (BBC Radio 4, 22 August 1997) went so far as to describe ethics as "the lubricating oil of science." The implication seemed to be that the purpose of ethics was primarily to ease the friction generated by initial reactions to the announcement of a new biotechnological discovery, so that in time we would come to realize that our fears or doubts were groundless. The example cited in support was that of heart transplantation, which at the time was greeted with much scepticism. It was argued that in 50 years' time people would no longer react against human cloning any more than they now do against human heart transplants. One day we would regard it as quite normal.

There are two problems with this attitude that biotechnological developments will inevitably be used, one logical and the other social. Logically it is nonsense, since we do not know the future one way or the other. There is not even a basis to predict with any confidence that the future will see the acceptance of a technology once doubted, like heart transplants, or the rejection of a technology once accepted, like nuclear power, or for it never to be adopted at all, like irradiated food. Indeed, the present mood of scepticism towards technology, compared with a generation ago, is in no small measure in response to the many problems which technology has brought with it. This factor is surprisingly overlooked in Matt Ridley's (1997) exasperation that we almost always react pessimistically to new technology, when he asks, "What harm has genetics ever done to justify the fears?" One would have thought that the human dilemmas imposed by having genetic disease information without a corresponding genetic treatment, or the animal suffering caused by some extreme selective breeding argued for substantial harm, even if the eugenic practices earlier this century had not already furnished examples enough.

More disturbingly, the assertion that the adoption of a given technology is inevitable is a self-fulfilling prophecy. It may be a false prophecy, but it would become true if we once believed it. Elements in post-modern sociology criticize science as a power game played according to the rules of one set of people who would wish to impose them on society as a whole, and predictably have been greeted with a storm of protest from scientists. Perhaps there is an element of truth in it after all? In the market place of ideas, what Egbert Schuurman (1980) has termed technicism is evidently alive and well.

WHAT CONTROL?

One factor to emerge from the overall reactions to Roslin's dramatic discovery and its enormous media exposure, is an undoubted call for better public accountability of current biotechnological developments. This needs informed public discussion which must be two-way, as opposed to scientists merely "educating" the public. It also needs a more open regulatory system. Ridley's (1997) assertion that governments should not regulate at all in this area, but should leave it all to the individual, seems to be out of touch with both the public mood and political and expert opinion, certainly in the UK and Europe. Examples are the House of Commons Select Committee on Science and Technology (1996-1997), the Council of Europe's (1997) new protocol on cloning, and the opinion of the European Commission's (1977) Group of Advisors on Bioethics are unequivocal as public statements, quite apart from the more humble declaration of the Church of Scotland (forthcoming) regarding this piece of indigenous technology on our own doorstep. An international ban on cloning human beings is surely an important marker to put down, even if it may be less effective than ethical self-regulation on the part of scientists. The fact that the Roslin scientists have repeatedly declared their opposition to such work is itself an encouraging sign of responsibility.

CONCLUSIONS

It seems there are good reasons to draw lines against cloning human beings, which leave open for the time being the uncertain possibilities which may arise from lesser applications of the techniques of nuclear transfer or embryo splitting. Cloning for animal production is more contentious, but this paper has enunciated reasons why in most cases a line should be drawn here also, on the grounds that this is carrying commodification too far, while leaving space for indirect animal cloning, such as Roslin's own work on novel genetic modification methods. But what is without doubt is that we should not be deluded by circular arguments that we had better lie down and accept that these things will happen anyway, because they need not if we do not wish them to.

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