Ethical challenges in embryo manipulation

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The more that is known about the development of the early embryo, the process of fertilisation, and the nature and specific functions of the cells' gene systems, as well as the environment necessary for them to divide and multiply, the greater are the possibilities of manipulating these embryos, whether in utero or in vitro. If we are prepared to make a fairly simple minded distinction, we may ask two questions: firstly, Should this knowledge be pursued? and secondly, To what use is it right or expedient to put it if we acquire it?

The questions may be distinguished and discussed as if they were quite separate. But it ought to be understood that in practice they are not completely distinct. Knowledge and using knowledge are not in reality two totally different things; or rather, acquiring knowledge and using it are not two totally different activities. In acquiring scientific knowledge possible uses for it often become apparent, and in making practical use of the knowledge we have we often acquire further knowledge.

Nevertheless, treating the first question separately and asking should knowledge of the early embryo be pursued, the answer seems to me straightforward. The rate at which new information, including information about human gene systems, is being accumulated is prodigious. There is a sense of vast new fields opening out to be explored. It would be impossibly arbitrary for someone to say, "Let nothing more be discovered." Even if on some principle an organisation such as a church or scientific funding council decided that knowledge would stop here, just where we are in 1991, such an organisation could not ensure that nothing more was discovered or published. And if someone were determined to pursue research contrary to the edict they could rightly plead, if challenged, that academic freedom is one of the highest human values and that to refuse to allow any increase in understanding of the world is contrary to one of the most important moral imperatives to which humans are subject. In short, to suggest that knowledge should be ossified at a particular date is a suggestion that neither could nor should be taken seriously.

Fear of knowledge

The fears people express about knowledge are mostly fears of the uses to which knowledge may be put. But it is worth considering whether an increased knowledge of human genetics, developing as it will out of our knowledge of the early development of the embryo and of the human genome "map," will pose any moral problem in itself. We may want to know more. We may encourage scientists to help us know more, but will our new knowledge be awkward for us to handle, whether we use it or not? The oddity of this question confirms the artificiality of the distinction between having and using knowledge. Many people believe that there are already problems: that we already know too much to live comfortably with our knowledge. After all, our language is based on the presumption that we voluntarily and deliberately do things: I kick, I bite, I scratch, I buy, I sell, I walk, I run. I am the agent. We are committed linguistically to

distinguishing what I do from what is done to me or what just happens. Moreover we deploy the optative mood, saying things like, "If only I hadn't done so and so," with the strong implication that I need not have done it if I had chosen otherwise. I blame myself. I express regret for something I have done but might not have done. And so we come to specifically moral language in which praise and blame are accorded for the things people choose to do. We take it for granted that we can be held responsible for our actions and that the will is free.

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But now we are being asked to accept the proposition that more and more of our non-freedoms can be revealed. Even if no changes in our genes were permitted we would know that they could be undertaken; and if we knew that they could, would not all ascription of responsibility, and thus all morality, fly out of the window? It is this kind of consideration which weighs with people who argue that we should not know more. Let us go on with our old assumptions and not rock the boat we've always been in since language and morality began.

Freedom of will

The first thing to say about this kind of argument is that, though people raise something they see as a great new problem, it is not new. Philosophers have worried about the freedom of the will for centuries. Factors inimical to human freedom have always appeared one after another. The omnipotence and omniscience of God was once thought to be a difficulty for freedom. Nature itself was another (for example to Aristotle). The neurophysiology of the brain has seemed to make freedom impossible and so have the workings of the unconscious. And we have known about chromosomal disorders for ages, some of which seem to make us less than free to choose how to behave.

The difference between past and present debates about freedom is that in the past we could do nothing to change the obstacles that stood in the way of the free will, or at least we could not do much. Nothing could change the will of God if He had destined you for ruin; and though people attempted electric shock treatment or surgery to change people's brains and so their behaviour, they did not seem sure exactly what they were doing. But now the very words "manipulation" and "engineering" seem to pose a threat. The information we shall acquire will be precise; and we know what alterations have already been effected by genetic engineering in plants and animals other than humans. There is thus a belief that not only are our actions, thoughts, and feelings programmed to be as they are but that the programme can be rewritten.

I do not believe that there is any reason to be appalled by determinism, whatever system of explana-

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Few would disagree that this child would be better off if she didn't have cystic fibrosis

tion for human conduct we adopt. For the bugbear of determinism is, and always has been, that if our actions and reactions are predictable they cannot be ascribed to us; we are no longer the true agents. Thus it is thought that in the light of determinism we must somehow lose our power to choose and to manage the world according to our wishes or our visions. Yet if we think about the nature of human choice we must recognise that, though what people want and choose may in some sense be explicable, it cannot be completely predictable because of the innumerable contingencies (including the detailed history of the agent) within the context of which a choice is made. Suppose that I think one evening, "I'll have scrambled eggs for supper." I go to the larder and find that the eggs are finished but that unknown to me someone has made some soup and left an invitation for me to use it up. You may think it likely that I will have soup. But unknown to you I have had soup for the last three nights and I'm tired of it. So I go to my car intending to buy some eggs before the shops shut. But unknown to me my car has been stolen. . . . The story can go on, and at each stage my decision about what to do is made in the light of the new circumstances. In the end of this exhausting history I may settle for the soup. Or I may be too tired to eat. Only if all the contingencies, as well as all my predispositions, prejudices, and tastes could be charted would it be possible to predict the outcome of the story. And if this is true about trivial choices such as what to have for supper, so it is of more important (so called moral) choices.

If everything were known and if I lived in laboratory conditions where the contingencies and chance happenings could be kept on record from the moment of my birth, then my choices might appear foregone conclusions if anyone could be bothered to draw them. But we do not live in such conditions and never could. We could never know all that had happened in the past to influence me, nor what was even now happening to limit or guide my choices. We feel free because we act against a background of ignorance, including ignorance of our own genetic system and of the input of circumstances and environment on the computer that is our own brain. Spinoza said that freedom was the ignorance of necessity. I believe that this is true and that such ignorance is the inevitable background against which we thrive. Being conscious, we are aware of what we want and how things seem; and, as important, we can communicate this more or less

successfully to one another. It will always, therefore, be quicker and more efficient to ask another human why they did what they did or what they are going to do in the future than to try to work it out by consulting a neurophysiological or genetic print out, even if we had one. It is the combination of consciousness, ignorance, and language which make up what we call freedom of the will.

I do not deny that greater knowledge of the human genome might change our views to a certain extent about the appropriateness of praise and blame or the efficacy or justice of punishment. But there are many factors which might make us wish to revise our views on these subjects, and the possibilities arising from the future of genetic manipulation are only one of them.

Use of knowledge

Thus I am not much put out by a new version of determinism. New knowledge in itself does not seem alarming. But manipulation is a different thing. Fear no doubt attaches to the possible uses of such precise knowledge as we now have and shall increasingly have in future because of the suggestion that other people, and not we ourselves, may be able to choose how we shall be. And so we come to my second question: To what use is it right to put the new knowledge we acquire?

In addressing this question it is necessary to draw certain preliminary distinctions, doubtless familiar to this audience, but necessary none the less if general arguments are to be put forward. We must first distinguish between genetic diagnosis or analysis, which may be carried out on the cells of an embryo either in utero or in vitro, and gene therapy, which is the replacement of a defective gene by a harmless one. Within the second category, a further distinction must be drawn between germline and somatic cell therapy. I am in no position to discuss the scientific differences between these techniques or possible techniques. There are, however, certain moral differences which may be thought to exist between the various uses to which increasing knowledge of the human genome and increasing technical skills may be put.

Some disorders in humans are single gene disorders, many more are polygenic, and more still arise from a combination of a polygenic system with environmental factors (such as diet). Most characteristics of humans which are not diseases but in which we are profoundly interested, such as musical ability, beauty, or a good memory are polygenic and doubtless also have an environmental aspect. Manipulation of embryos either to select for these characteristics or to intervene actively to produce them is, so far, beyond the bounds of possibility. Yet it is this kind of knowledge that is most feared by the general public.

A theoretical matter needs to be considered here. To what extent is it the duty of philosophers to look beyond what is now possible, and, considering the future, to say, "If this ever became possible it would be wrong?" To what extent may moral questions be blocked by simply saying that such and such cannot yet be done? Philosophers have always taken unreal, imaginary cases and tried to deduce from them what in general is right or wrong, coherent or incoherent. Plato, for example, using the myth of Gyges's ring, which would render its wearer invisible, raised the question whether there are things that are intrinsically wrong or whether the wrongness of any act is simply in the eye of the beholder, who in this hypothetical case did not exist. Was anything to be permitted if only it were unseen? This sort of argument is not made less interesting by the observation that Gyges's ring does not and could not exist. For it is an inquiry about principle not about fact, the ideal rather than the real.

There arises here a distinction between a truly moral or ethical argument and one which is concerned with legislation (and I shall return to this distinction later). For a moral argument it is inadequate to say, "This may be a problem for our grandchildren; it is not a problem for us" and to leave the matter there. If, on the other hand, we are concerned with what may be good and necessary (and morally based) law we may have to say, "This is adequate for the time; our grandchildren may have to revise it." Law must be based on a principle but that principle, though in accordance with morality, may need for practical purposes to be less thoroughgoing, more pragmatically limited, less speculative than a principle of morality itself. As I believe that some of the issues raised by the use of our new knowledge of genetics may have to be the subject of legislation, I think that some kind of compromise is needed between considering only what is now being done in genetic manipulation and trying to take into account speculations which seem so far to have no basis in reality. This may seem a rather feeble solution that does not solve any theoretical dilemma. Nevertheless, it does perhaps accord with another principle, which is that morality is based on human experience, human likes and dislikes, and these cannot be considered if we take off too far into the realms of fantasy. If the moon were made of green cheese who could say what my view of the world would be?

Prenatal and preimplantation screening

To return then to our initial distinctions: genetic diagnosis was first used in pregnancies in which there was a high risk of the embryo being affected by a monogenetic disease. Screening was carried out in the second trimester of pregnancy, and an abortion was offered if the fetus was affected. Chorionic villus sampling meant that fetal material could be sampled much earlier in the pregnancy; the danger to the fetus was less and abortion could be carried out at a much less traumatic stage, from the mother's point of view. The logical next step from here is preimplantation rather than prenatal diagnosis, when several embryos are fertilised *in vitro* and only those found to be healthy implanted. The drawback is the relatively low success rate of *in vitro* fertilisation and implantation. An alternative would be to flush out blastocysts from the uterus and reimplant those unaffected by the genetic defect. The avoidance of abortion in both these techniques is a desirable feature for a couple who want very much to have a healthy baby, perhaps having already had a child with, say, cystic fibrosis.

I cannot see any possible moral objection to such procedures. There may in some cases be clinical objections: perhaps a specific mother might be better off not to embark on a pregnancy or further pregnancy rather than risk the possible disappointments of *in vitro* fertilisation or repeated abortions. It could be argued too that there are economic objections, particular to the use of *in vitro* fertilisation. Otherwise, to attempt to ensure the birth of a healthy baby seems to be morally a wholly admirable aim.

Two arguments are, however, sometimes put forward on more or less moral grounds against such interventions. The first is, I suspect, trivial. It is now possible either at a very early prenatal stage or at preimplantation to find out the sex of an embryo and thus to abort or not implant an embryo of the sex not desired by the parent. There is an obvious case for selecting female embryos when there is a risk of, say, haemophilia (for even if the female were a carrier, her children could in turn be screened when the time came). But many people fear a slippery slope: that couples may demand sex screening followed by abortion of the female (or implantation only of the

male) embryo. And this is regarded by many as moral outrage, or perhaps a potential social disaster. I am seldom convinced by a slippery slope argument as it seems to me always possible in principle to block the slope by legislation at any point where society believes further descent would be outrageous or disastrous. Thus it would be possible to permit doctors to carry out sex selection only in cases of a threatened male-only disease.

But even without such draconian solutions it would be possible to ensure that sex selection would be carried out on the NHS only in clinically desirable cases. And if other cases were permitted in private practice I cannot myself see that much social or moral harm would follow. If a couple had three sons and wanted a daughter, or three daughters and wanted a son, what ill consequences would follow? Not everyone would be able to afford such luxury of self indulgence, it is true. But it would not constitute by any means the worst kind of inequality, even in medicine. I am not so modest as to think, as I have been told, that if people could choose which sex their children could be they would always choose boys; nor do I think they would be so short sighted as to do so. I am intrigued by the extent to which people seem to object to sex selection on non-medical grounds. I have not been able to discover the basis for such an objection. But if need be I could be persuaded that intervention at the embryonic stage should be only on approved clinical grounds. If this were to be incorporated in law or guidelines then further regulation specifically to prohibit sex selection on social grounds would be unnecessary.

The second objection to intervening at the embryonic stage is more complex, perhaps, and needs more urgently to be answered as it would, if allowed, call in question all intervention, even that carried out on plainly clinical grounds. This is an objection often voiced by what can be referred to as the handicapped lobby. They argue that if preventive intervention at the embryonic stage is permitted, whether by aborting defective embryos, selecting healthy embryos for implantation, or perhaps one day by actual gene replacement, this will downgrade those people who have been born with disabilities or who have acquired disabilities during their lives. Society, in permitting such interventions, is supposed to be saying to the handicapped, "We wish you had never been born." Such arguments are often put forward with varying degrees of passion by, or on behalf of, those who have mild defects: and this is the first thing to be said. Intervention of a preventive nature is, so far, aimed at the abolition of a few disastrous diseases which have a fatal outcome or which cause an intolerable burden to the sufferer. To try to prevent the birth of children with such diseases is not to imply any general thoughts about the handicapped, many of whom undoubtedly lead tolerable and indeed enjoyable lives and for whom undoubtedly more could be done to make their lives better. The same is simply not true of children with Duchenne muscular dystrophy or cystic fibrosis. The mildly handicapped are not properly entitled to speak on behalf of these children or their parents.

There is a second confusion in the argument, which I must now try to unravel. Let us suppose that I say of myself (for example, to my mother, who has told me that she had hoped for a boy), "It would have been better if I hadn't been born." I might imply by this that it would have been better (for my mother) if someone else had been born instead—namely, a boy. I do not identify myself with this unborn hypothetical boy. He, if he had existed, would have been a different person. I would not have existed, and I am saying the world would be in some way better if I hadn't. Now contrast this with a case where I say, "It would have been better if I had been born with longer legs." Here I can imagine

myself, the very same person, without a defect I have got—namely, short legs. There is a continuing thought of “I” in this proposition, but a recognition that, sadly, the “I” that exists could have been better in some ways. Now let us take two general propositions which I think are parallel to the last two. Firstly, it would be better if handicapped children were not born, but other children were and, secondly, it would be better if children were not born handicapped. In each pair of propositions, the first can be seen as a kind of reproach. The whole existence of the people in question is a matter for regret. The world would be better if instead of them, some other, superior, people existed. The second also expresses a matter for regret, but a regret that can be shared by the persons with the defects because those persons are imagined still to exist, but exist less defectively. Of course if someone has been born, to say, “It would have been better if, instead of you, someone else had been born,” is harsh. But I do not think that this has anything to do with the wish that parents may have before anyone at all is born, that they may have a healthy rather than a fatally handicapped child. For when the healthy child is born there is no other child. The other potentially handicapped child never did come into existence. To choose this situation is not a reproach to any existing person at all. For the healthy child who is born is in no way identical with the handicapped child who might have been born (just as I am in no way identical with the hypothetical boy who was not born in my stead). So I cannot believe that aiming for healthy children by embryonic intervention is a reproach to any existing person. The preference is for existing healthy children over non-existent defective children.

Germline and somatic cell therapy

If we take the second sentence, “It would be better if children were not born handicapped,” then we are saying that those children who do exist could be envisaged as better off than they are; a proposition few would deny. This statement is hopeful only if there is some way in which the lot of those people could be improved. And so we move from the notion of diagnostic (and preventive) genetic interventions to that of gene therapy, the actual remedying of genetic disease by means of gene replacement. Here the distinction between somatic cell therapy and germline therapy is, as I need not remind you, taken generally to be all important; and it is generally assumed also that gene therapy, when it becomes possible, should be carried out only at the somatic cell level. Somatic cell therapy, however, is not strictly relevant to my subject as it can be done only on people who have been born with a monogenetic defect. The aim is to introduce non-defective genes into particular cells of patients born with an inherited disease to replace those which carry the disease. The complexities of such procedures are enormous. But however the problems are overcome, there are not generally thought to be moral objections to such therapy. In 1982 the American Presidential Commission produced a report, *The Splicing of Life*, which held that the incorporation of a gene to treat a disease in an individual was in effect no different from the repeated administration of the product of that gene, and that any additional risks could be justified by the severity of the illness of the patient. Presumably the development of the techniques of gene replacement should proceed in parallel with the development of preimplantation diagnosis and identification of genetic defects. In each case research ought to be concentrated on an agreed list of inheritable diseases whose outcome is likely to be extremely bad. And this is indeed what is happening.

Unlike somatic cell therapy, germline therapy could

Biopsy for diagnosis of inherited disease in human preimplantation embryo 3 days after fertilisation in vitro. An embryo at about the 12 cell stage is being held still by suction on to a glass micropipette while another micropipette is pushed through a hole dissolved in the coating around the embryo and a single cell removed by suction. (Courtesy of Dr A H Handyside, Royal Postgraduate Medical School funded by the Muscular Dystrophy Group)

in principle be carried out by altering cells in early embryos or in the fertilised egg. Such transgenic mammals are already used for research purposes, and the techniques could be used on humans. This form of gene therapy reaches all the cells of the organism, and the genes thus altered are themselves heritable. Though all monogenetic diseases could in principle be treated in this way, the new genes do not replace but add to the defective gene, which would thus be likely to recur at some stage. The main reasons for rejecting germline cell therapy for humans, however, are not that it is ultimately ineffective and is difficult to carry out but that it is unpredictable and its consequences seem to stretch on for ever. If this is so it seems to me hard to say where one would draw the line and regard what happened as a consequence of such intervention. It might be possible to say in a hundred or two hundred years time that a certain mutation would not have occurred if we had not engaged in germline manipulation; and thus we should be held blameworthy by future generations. But it is not clear how long this responsibility would, or should, be ascribed. At the same time it is impossible now, where we stand in 1991, to carry out the ordinary utilitarian calculations of benefit and harm, when we neither know how long the effects would be ascribed to present intervention nor have any clear idea of what those effects might be. It is sometimes said that germline therapy should be forbidden because we would take the processes of evolution into our own hands. This does not seem to me a conclusive argument. We are always doing that, in more or less conscious ways, by contraception, for example, or by trying to limit the number of babies born with heritable diseases through prenatal or preimplantation diagnosis. The most serious argument against germline therapy is our present ignorance. And I therefore believe that if we knew more we might think it right to undertake it in certain prescribed circumstances. If, for example, it became possible to eradicate immune deficiency diseases, in particular AIDS, through germline therapy the advantage might seem sufficiently great to outweigh the argument from ignorance. I would not therefore wish to rule out forever the legitimacy of germline genetic manipulation at the embryonic stage. The real horror that people fear is that of genetic engineering used to produce humans to a design of some dictator or political tyrant.

The slippery slope

We come then to the question of how to block the slippery slope: how to bring into force regulations that will ensure intervention that is beneficent not harmful and that does not go beyond what people think

reasonable. Here is, of course, the most intractable moral problem of all. It is not so much a question of what is right or what is wrong as of how such distinctions are to be made. If we lived in a theocratic society, where certain priests, elders, or ayatollahs were supposed to have direct access to divine commands, the question would be easy to solve. The question of intervention at the cell stage would have to be put to only these experts, who would come up with an acceptable answer. But in a democratic society with a mixed and hybrid system of morals and no recognised moral experts but instead, if anything, a Protestant belief in the sovereignty of the individual conscience it is different. Let us take the relatively simple case of preimplantation diagnosis of hereditary disease followed by selective implantation of healthy embryos. Research using human embryos (subject to time limitations) and in vitro fertilisation are permitted by law; the rights and wrongs of that need no longer be a subject of public debate, even though there are and will remain some who are opposed to them. There is still the question, however, of what conditions should be researched and treated by these methods. Is it tolerable to society that public money should be spent on the alleviation of just any conditions?

It seems clear from the foregoing argument that there must be a barrier placed on the slope so that we do not slide down into what many regard as the frightening place where people can choose for themselves, or, worse, have chosen for them what sort of people there should be. We therefore need an agreed list of conditions into which research should be encouraged and for which preimplantation selection of embryos (or prenatal selection) should be permitted without question. There is a long list of monogenetic disorders that can be detected and that, after an analysis of family history, could be diagnosed in the embryo. It is therefore easy to imagine a list of disorders which could form the agreed targets of research and treatment (and of course the more successful embryonic selection became, the less need there might be for contemplating the more dubious techniques of germline therapy). Even so it is also easy to envisage a time when the question, "What conditions merit treatment?" might have to be faced. Such a question might be partly financial, a matter of priorities within a research or therapeutic programme, or partly a matter of values: what diseases are so manifestly intolerable to those who are born with them that we must at almost any cost try to prevent such people being born? Both aspects must be settled in a way that will command general respect and agreement.

There are inevitably differences between moral judgments made in the private and the public domain. In private someone may adopt a moral principle and decide to stick to it, though the heavens fall: he may martyr himself to a moral cause and be admired for doing so, even by those who do not share his moral convictions. An ethics committee can not martyr itself. It has to work out what will on the whole be for the best: what will not outrage too many people and what would quite obviously be going too far. These are ways of settling moral issues, but they are mundane and non-heroic ways. Yet settling an agreed list of diseases for which embryo manipulation may be employed

must, I believe, be done by committees not individuals (though of course no individual needs to agree with a committee decision, nor need any individual have any part in practices he or she feels to be morally repugnant). For such issues are essentially and not just accidentally matters of public policy, over which we believe there should be control but not control by any one person.

Some of the issues that arise in connection with embryonic manipulation seem to be settled for the time being at least. We need not, mercifully, go back to the debate about whether embryos less than 14 days' gestation are to be treated as people. The moral question having been settled one way, the law has now clarified the issue. Yet both genetic diagnosis and genetic therapy still give rise to moral questions, which are fundamentally questions about power; who should exercise it over whom?

This is a common form of moral question, but in the case of embryonic manipulation it is a question asked in the public domain. We are talking about generalities within society, not about individuals and their relationships with one another; and therefore the question is essentially political as well as moral. Any attempt to answer it must therefore concern itself not only with the ideal but with what is possible. If, as I believe, legislation is necessary to control and regulate the uses of our new knowledge of the human genome and the associated technology, then the legislation must be based as far as possible on moral consensus, otherwise it will not get through parliament, or if it does it will be incapable of being implemented.

Part of the moral issue then is not what is right and what wrong, but how can an agreement be reached on what is right and wrong. It is commonly presumed that ethical or moral questions can be solved by hard and clear thought and that moral codes based on such thought can ensure a correct way of behaving in a given situation. Both presumptions are false. No group of philosophers, however clearly and hard they think, can arrive at a correct solution to a moral problem as such problems do not admit correct solutions. For morality rests not just on calculations and reasoning but as much on traditions, feelings, scruples, and reluctances. Nevertheless, despite the inexact nature of moral judgments if an advisory committee is set up to examine moral issues and to suggest solutions it may command respect, even agreement, provided that its deliberations are open and its conclusions based on knowledge rather than ignorance. The recommendations of such a committee may therefore produce useful guidelines for public policy in medical and other contentious matters. But this is all and the best that a committee can do. Its conclusions may arise out of a certain discovered consensus, and may give rise to a wider consensus when its guidelines are in place. But it can never produce certainty. Certainty (albeit of a different kind from that sometimes looked for from philosophy) can be produced only by legislation. And it is for this reason that I believe legislation may well be required in some of the areas of possible human genetic manipulation. For the difference between the non-criminal and the criminal, the permitted and the impermissible is at least clearer and more definite than the difference between right and wrong.