The Genetic Revolution

Cloning animals is routine

A science fiction nightmare has been giving people the power to create carbon copies or identical twins of themselves.The technology is already here and so are growing concerns about its use (60).It is in fact far easier to just copy all the genetic code of a cell than it is to rewrite it.Even easier than copying is to get the body to do the copying for you.Since all cells in the body except red blood cells and germ cells have an identical nucleus containing all the individuals genes, we have an unlimited source of complete chromosome set we can use.Even simpler, we could transplant the entire nucleus from one cell into another using a microfine glass pipette (see p for how they are made and used).For many years, we have been able to clone animals including pigs, sheep, rabbits, cows and chickens.In fact we seem able to clone just about any mammal we have turned out energies to cloning.

To produce a clone, we need to be able to get hold of a complete set of chromosomes and put them into an egg and see what happens.A frog's egg is easy to do this on because the nucleus, seen as a black dot, in unfertilised eggs in fresh frogspawn is so large. As we have seen, the nucleus removed contains only a half set of chromosomes of course and would not give instructions to divide until the half is provided by a sperm at fertilisation.

Cloning techniques

However, with somewhat greater difficulty, we can borrow a complete set of chromosomes by taking a whole nucleus out of a skin cell.The skin nucleus is very small and the procedure is not easy.If we now inject the skin nucleus into an egg (nuclear transplantation) then a remarkable transformation happens (70):the nucleus wakes up to the fact that it is no longer in a determined cell, and pulls all the volumes of the encyclopedia off the shelf at once.The nucleus instructs the cell to divide and divide again repeatedly until the call of the cell starts to influence itself with each cell touching other cells beginning to fix its role for the future according to its position.

Interestingly, if you want to save all the fuss and bother, you can make yourself a cheap cloning system by separating individual cells off before the big ball develops.If you do, each single cell taken away will carry on as if it is the only cell in the world and will go on dividing like a brand new fertilised egg.This technique is called blastomere separation.

Cloning animals is routine

Robbing early dividing groups of cells to produce clones has worked well recently for a variety of animals, especially cows and sheep (70).Why bother to mate a magnificent prize cow with a bull which will add extra genes you may not want?Why not just clone the freak high output high meat yield cow and insert these egg-like dividing cells into dozens of other cows to act as surrogate mothers for the clones?Why not indeed?Farmers have felt there are so many good reasons in favour that cloning is now set to become a standard breeding technique.

The days of prize bulls or stallions mating or even donating sperm may be numbered.Any animal can in theory be cloned this way.Obviously, it takes a lot of skill to detach healthy dividing cells after fertilisation and insert them into wombs at the right time and there is a limit to the number of clones you can make for each fertilised egg (80).We used to be able to work this method only up to the eight cell stage in mammals (90), but the limit is growing all the time (95).The reason is that until the developing ball of cells has properly implanted, each time the cells divide, they tend to get smaller, with less food reserves remaining in each.Taking one call out of the ball to form a new ball is going to result in a smaller second ball of cells and a weakened embryo which may not be viable.Many of the techniques being used here - for example invitro fertilisation and embryo replacement, have been routine in infertility clinics and in farming for a number of years.

What about cloning humans?

So what are the practicalities of cloning humans?I have met a scientist who claims he has already cloned a human embryo (100).He found his embryos were dying very early - I suspect because he was using animals as surrogates and the surrogates were rejecting human embryos.

So is there a market for human clones?I am deliberately asking this question laying aside any ethical considerations for the moment.The question is important here and in every other level of genetic engineering.If there is a market then I expect it will happen somewhere.Legislation, as we will see, may not protect unless it is effective and global.If there is no market it may still happen probably, but probably on a more experimental scale limited only by the conscience of the experimenter.

Unfortunately, global experience in war and peace shows us that such vast cultural and individual differences exist in world view and personal ethics between individuals and nations that I regard it as inevitable that somewhere at some time scientists will pursue what is physically possible.To some extent such exploration will be for its own sake but no doubt driven by whatever are their own moral, philosophical, religious or political persuasions.

The market for human clones could be huge - especially if they can be frozen (and they can) and only produced some years after the death of the clone donor.

A child with built in guarantees

After all - and I am being deliberately provocative - if couples can opt for a donated egg and sperm from parents with known characteristics, to be inserted into the mother's womb, why not cut out the uncertainties and go for a child with a set of guarantees?

guaranteed intelligence,

guaranteed free from genetic diseases,

guaranteed abilities in other areas.

You could even have a photograph showing what the child would look like aged 2 and 6 years old.

The only thing that would not be guaranteed would be the right environment for the child so that his or her genetic potential could flourish best.However, we could also describe a guaranteed environment as one which has tended to produce excellent results with this set of genes in the past.

Dictators in the past wishing to guarantee the survival of some aspect of their own personality have only been able to resort to conceiving a large number of children.Cloning could be very appealing - possibly "irresist -ibly" tempting to a dictator wanting a son and heir worthy of his destiny.For someone possessed with a sense of his own self, it could indeed be a fascinating adventure to watch himself grow up again in a different situation.

Let us argue for the sake of exposing the controversy that it is in fact no different from having a child who seems to have naturally inherited vastly from one parent:"He is the spitting image of his father".

What is so unnatural about twins?

Here is another thought: would you be able to spot a clone if you met one?The answer is probably not unless you are a member of the same family and have access to the photograph album.It should be pointed out here that identical twins of course have a totally identical, genetic code and are clones of each other.

Triplets are also natural clones.In our example of adult cloning, the only thing that makes it unnatural is that the identical embryos are not born at the same time but possibly fifteen, twenty or even fifty years apart.The other difference is that they would be born with different parents - or apparently so.

It could be argued that since environment does have such a huge influence on development, the only identicalness would be in appearance at each stage compared to old photographs of the clone donor.In fact, due to age differences, donor and clone will probably never even look identical.Even if they are similar in age and look and sound the same one might ask what is so unnatural anyway about twins?Natural clones exist therefore in virtually every family tree.

Please understand that I am not arguing myself from a point of personal conviction, but unless we understand the ways these issues are likely to be presented then we will be wholly unprepared to meet the issues of tomorrow's world - a worl approaching faster than we ever realised.Genetic engineers are swift to point out technical difficulties but in fact they are no different from the difficulties of cloning any other mammal.However the ethical difficulties are vast.

New Parts for Old Bodies

These is another more hideous (yet also potentially lifesaving) aspect of cloning: using a clone to manufacture a new organ.Earlier we saw that cells in an embryo quickly sense their position in the body and become more and more specialised.In theory it should be possible to take a semi-specialised cell developed from a fertilised egg and treat it in the laboratory so that it reacts to form, say, a perfect replacement kidney.A simpler approach already being used in medicine is to collect aborted foetuses in a bucket in an operating theatre and then surgically remove various organs and tissues for transplanting into people who need them.Needless to say the practice, although common, has not been widely publicised.

Why is there a demand for foetal or clone transplants?

Spare part surgery only works if spares are available, and if spare parts work after replacement.Unfortunately for many who die each year of kidney, heart or other organ failure, not only are spares often not available but they also often fail to work.

Spares are often unavailable because tissues or organs need ideally to be moved instantaneously from one living body into another.The nearest we get to this is the living donor: a parent who donates a kidney to a child for example.In these cases, two surgical teams operate at the same time on donor and recipient in adjacent operating theatres.

In many cases, where an organ could be donated, death has occurred with loss of circulation and accumulation of poisonous substances before tissues can be removed.In the case of donated corneas or skin grafts the timing is not critical.Corneas survive body death for a number of hours.

Their need of food and oxygen is low and transplants are relatively straightforward.Kidneys however work extremely hard at all times in the body, purifying the blood.Kidney cells are damaged permanently in half an hour unless the kidney is rapidly chilled after removal by storage in an ice box.Kidney donors tend therefore to be accident victims where massive brain destruction has occurred, the person is effectively deceased but the heart, lungs and kidneys are all still functioning, with machines artificially maintaining the body in the twilight zone between life and full death.Kidney donation is therefore accompanied by a temptation to turn off a life-support machine.The numbers of kidneys available fell dramatically recently after a series of television programmes which caused great public uncertainties about whether or not such accident victims were truly dead.Fears that pressures to transplant could over-ride a small chance of recovery led to many relatives refusing to give permission and to large numbers of people tearing up their kidney donor cards.There is still an acute shortage.

However, even if sufficient organs available there is often a further major limitation of spare part surgery: compatibility of tissues between donor and recipient.

As we have seen, each person's set of genes is a quite unique combination of tens of thousands of individual messages.Just as each person's facial features are different, so also are the surface features of each cell in the body.The area where we are most familiar with this is that of blood group: there are several main blood groupings, each of which is incompatible with the others.For this reason blood type of both donor and recipient are always checked before transfu -sion.However, even if you are the same blood group as me, and were to donate to me a kidney, my body would almost certainly regard it as a foreign germ and try to destroy it.Very occasionally, you find two people whose cell features are so similar that a transplant would be accepted well.Finding these matches between all organ donors and people needing them is therefore extremely complicated and explains why organs are often flown great distances to find the person with the best "match".It also explains why commercial pressures have resulted in buying and selling kidneys, and in paying non-relati -ves to donate them.Genetic engineering is contributing to our understanding of these cell differences and how to overcome them (110).

Badly matching organs usually fail rapidly although some help can be given by giving high doses of steroid and other treatments to try and persuade the body's defences from attacking the transplant so vigorously.

So spare parts are often not available and often do not work as well as we would like after a transplantation.Having said this, we are seeing great improvements with more sophisticated treatment after transplantation and a great many alive today owe their survival to organ donation.The two which perhaps do best are kidneys where kidney failure itself poisons the body's defences so transplant rejection is often less and cornea transplants where the body's defences seem to tolerate new eye coatings very well.

Spare part production using new technology

Having decided there could be a big market in self-grown replacement organs, how would it be done?

First we have to look at what has already been carried out in animals or using animals.In 1984 there was a huge outcry when a surgeon in Southern California removed the beating heart from a baboon and transplanted it into a baby known as "Baby Fae".For reason which are obvious from what we have just seen, the heart was rejected and the baby died.However we are now seeing similar experiments in reverse: organs removed from late human foetuses that have just been aborted, and inserted into animals.

These experiments are being carried out in Palo Alto Mexico by a company called Systemix backed by a $11 million investment (120)They are using mice bred without any natural immune system to fight either infection or transplants from humans.They are kept in a strictly germ free environ -ment.Then they receive human tissue - for example thymus, lymph node or liver cells.With these transplants the mouse develops a human style immune system.The mouse can then be infected with the AIDS virus (HIV) or with other viruses which also fail to grow well other than in humans.The mice can then be used to test potentially hazardous new treatments.These humanised mice are big business but may be flawed because mice still do not produce disease like we do.

Incidentally, there is another more serious problem: trying to infect mice with HIV could lead to a mutation producing an even more dangerous version of HIV.This could happen if mouse viruses combined in some way with HIV.It has even been suggested by some scientists that such inter-species virus experiments could conceivably have led to the emergence of HIV in the first place (130).Although the evidence appears to be stacked against this alarming suggestion, the fact that it can even be made shows some of the problems that can emerge.As we will see later on, experimental viruses have combined unexpected -ly with each other in animals in the past, becoming more dangerous as the new strain emerged (135).

Foetal transplants for humans

We can reverse this method to treat humans: how about taking organs or tissue from animal foetuses and transferring them into humans?Such transplants will be as surely rejected as the monkey heart in the earlier example. But what about removing tissue from an aborted human foetus and using that instead?Such an idea is abhorrent to me and to most of the population but is it being done?

For several years now tissue from aborted foetuses has been used to treat patients with "severe combined immunodeficiency disease" (140).Unlike AIDS this is an inherited condition affecting all the immune system rather than just one part.The tissues transplanted are pieces of liver and parts of the bone marrow.In another related disease called the Di George syndrome, the tissue transplanted is from the Thymus gland (140).Other types of immunodeficiency, disorders of red blood cell production and disorders of metabolism can also be treated in this way.

Interestingly, although the foetal tissue is completely incompat -ible and would normally have been rejected - no matching takes place between foetal donor and recipient - these transplants seem to work (140).Other uses are likely to be made of foetal transplants in the future.Over the last ten years a number of experiments have been carried out in animals using foetal tissue transplants to cure brain damage.Such experiments are an extension of nerve tissue transplants that have been studied for around 100 years (145).If these latest experiments prove successful then we can expect to see foetal brain or spinal cord transplants in humans.The hope would be to try and overcome a big problem in damaged human brains. Unlike the situation in the developing embryo, once a baby is born the nerve cells seem to stop dividing and their response to injury is unlike other parts of the body.By using primitive brain cells we might be able to allow a certain amount of repair of the brain to take place (145).

So what about the future?

Let's take the case of a dying prize winning musician.He needs a kidney and none is available.He gives a blood sample and is told to come back in about eight to ten months' time for a transplant.He pays a very large sum for the privilege.The transplant is entirely successful.The only complication is that it takes quite a while to get going fully.

Without realising it, he has just paid a private clinic for a cloned kidney.A nucleus was taken from a white blood cell in the sample he gave, and it was then inserted into a human egg, which in turn was implanted into a surrogate mother's womb.After nine months, a cloned baby was removed by Caesarian section.Shortly after birth one kidney was removed and inserted into the professor.The baby was adopted 24 hours later by doting new parents believing that the child had been born naturally but with a defective kidney that had now been removed.

Fact or fiction?As we have seen the cloning technology is all there.The demand is certainly there.For the present there are two blocks: the first is obtaining a surrogate mother.However that is becoming easier in the West if the right story is told and is difficult to prevent commercially in the two-thirds world.A mother could be offered the equivalent of ten years wages (?10,000) by an agent.The second larger block is that a newborn baby kidney is much too small and immature to help a full-grown adult much.However, other tissues might do rather better, in particular bone marrow and other rapidly dividing organs such as skin to cover grossly disfiguring burns for example.

Perhaps having at least formed a complete baby kidney we will in the future be able to accelerate its growth in the laboratory using new growth hormones while connecting it to an artificial blood supply.

The skin example is an interesting one because we are able in this case to clone skin directly from skin cells - without having to create a whole new human being.Skin cells can be stimulated to grow and divide.They can be tricked into thinking that they are on the edge of the wound.In the laboratory large sheets of skin can be grown quite rapidly from just a few sample pieces of skin.These can then be returned to the donor.We are also able to clone cells successfully from bone marrow as a routine part of medical treatment in those with leukaemia.

The Genetic Revolution - free book by Patrick Dixon - published 1995