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Anne McLaren as Teacher

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Of all the aspects of Anne McLaren's work, there is only one with which I can claim familiarity, and that is her genius as a teacher. I first met Anne in 1982, when the then Government set up a Committee of Enquiry into Human Fertilisation and Embryology, whose terms of reference were *'To consider recent and potential developments in medicine and science related to human fertilisation and embryology, to consider what policies and safeguards should be applied, including consideration of the social, ethical and legal implications of these developments; and to make recommendations'.* We were given two years in which to complete this task, which seemed formidable; and by a miracle we presented our report on time. It would certainly not have been thus completed, nor would it have been so widely read and generally intelligible if it had not been that we had Anne as our mentor.

The method of setting up Government Committees of Enquiry seemed to me then somewhat ramshackle. (I am sure things are different now, and far more politically driven). Once a Chairman had been found (and of how this was done I remain ignorant), then consideration is given to what categories of people should compose the final committee. Though these people would not be representatives, in the sense of being responsible to their constituents, they would nevertheless be relied on to present things from a point of view that ought not to be overlooked. So, obviously, there must be at least one obstetrician, and at least one general practitioner. There must be someone with an understanding of Muslim law, since infertility is a serious issue and is a ground for divorce in Muslim society. There must equally be someone who was learned in English Family Law, and someone of the same kind for Scotland. We must have a Roman Catholic, to ensure that we could not be accused of neglecting the views of those who regarded all human life at whatever stage of development as equally valuable. (We were so accused, nevertheless. But in fact our Roman Catholic member, John Marshall, a Professor of Neurology, and a most helpful and hardworking committee member, wrote an admirable minority report, setting out his arguments with great lucidity). I remember being presented by senior civil servants in the Department of Health with a list of potential members in all of these categories and others. I vetoed one name (with great difficulty), and had to go direct to the Minister, to tell him that I could not work with this particular person. On the day before the publication of the membership was due, he rang up to ask why I could not. All I could say was 'He gives me the creeps'. But that was good enough, and someone else was found. In all this, the only thing I felt really strongly about was that we should have a research scientist, not a medical practitioner, who would be able to explain things to us. I was desperately aware that I had had a virtually science-free education, and that, though I had picked up a little hardly relevant information, while chairing the Committee on the use of animals in laboratories, it was a matter, in my case, of starting at the beginning. Back to Basics. The civil servants assured me that Dr. McLaren was just the person I needed, and would take me in hand as a pupil; and they were absolutely right.

Abbreviations used in this paper: AID, artificial insemination by donor; IVF, in vitro fertilization; M.P., Member of Parliament.

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The occasion for the establishing of this Committee was the general excitement and increasing anxiety felt by the public following the first successful IVF (*in vitro* fertilisation) birth in 1978. At first the press had responded with delight to this much-publicised birth; but doubts set in, and by the beginning of the eighties it seemed that here was an issue as divisive as that of abortion, and that some form of legislation was almost certainly required. I had learned from my experience on the Animal Experimentation Committee that the most satisfactory way forward was likely to be a system of regulation that would demand licensing. (Though in fact it took me some time to recognise how closely analogous the two issues were, both arousing extraordinary passions, and both therefore requiring a framework of law that would to some extent reassure the public that there were to be tight controls, with inspection and penalties in the background). However this general expectation with which I at least approached the task could not be turned into a practical recommendation, if it seemed to be based on ignorance or confusion.

One has to remind oneself how grossly ignorant most of us (that is the general public) were at this time. Soon after the first IVF birth, and when it became plain that if IVF were to continue it would entail research using live human embryos, a pressure group was established called Save The Unborn Child, an offshoot, probably, of similar anti-abortion or pro-life groups which had been in existence for many years. This group used as its logo a curled up fetus; and most people in the non-scientific world thought of the outcome of a successfully fertilised egg in terms of this image, a recognisable human animal.

It was Anne who introduced us to the facts, and thus to the concept of the omnipotent cells of the immediately post-fertilisation embryo; to the idea of the gradually developing 'conceptus', which becomes a recognisable embryo as the days go on; to the story of the growth of a cluster of cells into an entity which will become a fetus and then, with luck, a baby. I remember sitting at her feet as she explained, with infinite patience, and with unruffled amiability, with excellent diagrams, and impeccable clarity, the developmental story of the fertilisation and post-fertilisation development of the embryo, and thinking that if I had my life again I would be a biological scientist, or, more specifically a zoologist. I have never enjoyed a process of learning more.

I had great difficulty in deciding how to put together the report that was the outcome of our committee's deliberation. There were two main problems. The first was that we had been set up to consider issues that arose from questions of infertility. Yet it soon became plain that there were problems related to the possible regulation of such procedures as AID (Artificial Insemination by Donor), which were not directly related to infertility. For example lesbian couples might wish to make use of AID, borrowing sperm, sometimes, from gay couples who had sympathy for them, about whom the question of infertility did not arise. Again, there were Muslim women who sought AID without the knowledge of their husbands, because it was assumed in their society that failure to conceive was always the result of female infertility. If they did not conceive they were liable to be thrown out of the marital home without support. Such issues raised problems of regulation, of the proper screening of sperm-donors and of confidentiality which were enormously important, but not matters centrally concerned with infertility.

In the end, I decided to start by listing and discussing the possible methods of 'artificial conception', whether related specifically to infertility or not, and then proceed to an exposition of the scientific issues, the actual story of the development of the embryo. This may not have been the best approach. But I remember feeling a kind of fog of indecision about how to include all the issues in a coherent order.

In this decision-making process I have to say that I had less than useful help from the secretary of the Committee, who though agreeable enough, and an English graduate from Somerville, was helpless in matters either of drafting or of the general logical sequence of the report. My main help came from Anne, who saw the problem, and was, as usual, clear-headed and logical in her suggestions.

So what we did was to separate the question of methods of treatment of infertility, and the creation of new styles of family from the scientific issues, and the possible future outcomes of research using human embryos. I think this had a profound effect on our subsequent ability to get the report accepted and to get the Bill that was based on the report through both houses of Parliament.

It was in the exposition of these scientific issues that Anne's influence was paramount, ably assisted as she was by our scientific secretary from the Department of Health, Jeremy Metters, who was a great support.

I cannot do better here, I think, than to quote the crucial paragraphs (11.2-11.7) which Anne drafted for the opening of this section of the report. It gives a flavour of her style of teaching, her clarity, her non-intimidating manner which made the science available not just to the committee as it was deliberating, but to the wider public, crucially including Members of Parliament (MPs), who read it when it was published.

Early human development

11.2 *At fertilisation, the egg and sperm unite to become a single cell. The nucleus of this cell contains the chromosomes derived from both parents. This single cell is totipotential, as from it develop all the types of tissue and organs that make up the human body, as well as the tissues that become the placenta and fetal membranes during intra-uterine development. In vivo, fertilisation takes place in the upper portion of the fallopian tube and the fertilised egg then passes down the fallopian tube into the cavity of the uterus over a period of four to five days. At first when it reaches the cavity of the uterus, it remains free-floating until it begins to attach to the uterine wall at the start of implantation. This is considered to begin on the sixth day following fertilisation. During implantation, which occurs over a period of six to seven days, the embryo enters the endometrium, the lining of the uterus. At the eleventh to thirteenth day after fertilisation implantation is complete.*

11.3 *While the fertilised egg is still in the upper portion of the fallopian tube, it begins to divide into first two, then four, then eight, then sixteen smaller cells, and so on by a process called cleavage. At the start of cleavage, in a two or four-cell embryo, each cell retains its totipotential capacity. Thus if separation occurs at the two-cell stage each may develop to form a separate embryo. Such a separation could lead to identical twins.*

11.4 *When sixteen or more cells have resulted from cleavage the cells hang together in a loosely packed configuration, similar to that of a blackberry, called a morula. The morula stage is reached at about the same time as the embryo in vivo reaches the*

uterine cavity. At about the same time a fluid-filled space begins to form in an eccentric position within the substance of the morula. Once this accumulation of fluid had occurred, the embryo is described as a blastocyst. Within the blastocyst a thicker section of the cyst wall becomes identifiable as the inner cell mass; it is within this mass that the embryo proper, eventually to become the fetus, develops. The remaining cells of the thin walled portion of the blastocyst develop to become part of the placenta and fetal membranes. At about the time that the blastocyst begins to implant, a second fluid-filled space, the amniotic cavity, also appears within the inner cell mass. Between the two cystic spaces within the blastocyst, a plate of cells is formed. This is described as the embryonic disc; within it the first recognisable features of the embryo proper will appear.

11.5 *The first of these features is the primitive streak, which appears as the heaping up of cells at one end of the embryonic disc on the fourteenth or fifteenth day after fertilisation. Two primitive streaks may form in a single embryonic disc. This is the latest stage at which identical twins can occur. The primitive streak is the first of several identifiable features which develop in and from the embryonic disc during the succeeding days, a period of rapid change in the embryonic configuration. By the seventeenth day, the neural groove appears and by the twenty-second to twenty-third day this had developed to become the neural folds, which in turn start to fuse and form the recognisable antecedent of the spinal cord.*

11.6 *Once fertilisation has occurred, the following developmental processes follow one another in a systematic and structured order, leading in turn through cleavage, to the morula, the blastocyst, development of the embryonic disc, and then identifiable features within the embryonic disc such as the primitive streak, neural folds and neural tube. Until the blastocyst stage has been reached, the embryo in vivo is unattached, floating first in the fallopian tube, and then in the uterine cavity. From the sixth to the twelfth or thirteenth day internal development proceeds within the blastocyst while during the same period implantation is taking place. Both the internal and external processes of development are crucial to the future of the embryo. If the inner cell mass does not form within the blastocysts, there is no further embryonic development, while if implantation does not occur the blastocyst is lost at or before the next menstrual period.*

11.7 *Identical developmental processes are followed by embryos fertilised in vitro. In these, the first cleavage divisions will occur before the embryo is transferred back to the uterus. Thereafter, where implantation takes place the developmental process will be identical for in vivo and in vitro embryos, but there is a very high wastage rate in both as a result of their frequent failure to implant.*

I hope I may be forgiven for quoting at such length from our report. Almost everyone is acquainted with these facts now, and specialists had long been acquainted with them. But it must be remembered that for the ignorant members of the committee and for most MPs and other members of the public they were a total revelation. And to have them set out so clearly, with no technical terms used that were not defined was of enormous importance, both for us then and for others later. It was from these facts, when we had been taught to understand them, that we derived one of our central recommendations, now incorporated in the law, that research using human embryos might be undertaken up to but not beyond the fourteenth day from fertilisation. It was from these facts that we hoped to persuade Parliament that the development of the human embryo was essentially a gradual process.

This last point was of crucial importance. There was a strong tendency among the public (and I include Parliament, when it came to debating the issues) to raise the question *'When does life begin?'* Many people thought that if you could point to a moment when life did begin, then you could go on to argue that from that moment the embryo must be protected and might not be used for research, any more than a child or an adult might be so used. There were many who said that we should have a moratorium on research until scientists could show definitively when that moment occurred. I tried many times to explain that the question *'When does Life begin?'* was the wrong question. What we were really asking was *'When, in the gradual development of the embryo do we begin to think of it as something that merits protection? What, at its various stages, is to be its moral status?'* When this issue was eventually debated in Parliament, in the Bill of 1989/90 which began in the House of Lords, the most effective speaker to argue the developmental view was the then Archbishop of York, John Habgood, a lapsed biologist. (I remember an outraged elderly cross-bencher saying to me that no Christian could countenance research using even the least developed embryos. I said *'But the Archbishop of York was in favour of research',* and he replied furiously *'HE'S not a Christian'*).

We published our report in the summer of 1984.The embryology Bill started its course through Parliament in late December 1989,and was passed in 1990. During that period of more than five years Anne McLaren was tireless in her attendance at conferences, her lecturing and addressing audiences from school children to MPs, to explain to them, as she had to the committee, the science that lay behind our arguments. In the last chapter of our report we had more or less left behind infertility treatment and had cautiously looked ahead to other areas, such as the remedying of monogenetic diseases, where the new knowledge which would come from research using the early embryo might bring striking developments. And there is no doubt that Anne, sympathetic though she undoubtedly was to the plight of the infertile, was more interested in these aspects of the future than in anything else. In an intervention at a conference in Germany in the summer of 1989, when none of us had any idea what the outcome of the debate on the Bill would be, she cautiously opined that *'if debates in parliament and public opinion polls are anything to go by, the tide of public opinion is moving towards research rather than away from it'.* And she added that the Bill was *'more likely to be passed if there is a vote now than if there had been a vote three years ago'.* [Social Consequences of Genetic Engineering, Excerpta Medica Amsterdam-New York-Oxford 1989] She was right; and the credit must go largely to herself.

It was in fact conspicuous how much interest had shifted by 1990 from the treatment of infertility to the possible treatment of monogenetic disease, as an outcome of research using human embryos. Indeed there was a spirit of optimism among many members of the medical profession who believed that within five years we should see the replacement of defective embryonic genes, fetal surgery and other radical genetic manipulation. The Human Genome project was getting under way, and though Anne herself was cautious, there were many who expected great wonders in a shortish time.

Anne's caution, as well as her unfailing patience and courtesy in her treatment of the ignorant, was one of the features of her work which gave her most credibility. No one could accuse her of being the mad or irresponsible scientist. Whatever the possibilities were of gene replacement, she was at that time adamant that such novel procedures should be carried out only on the genes contained in somatic cells. She argued that we are, and will inevitably remain wholly ignorant of the long-term effects of intervention into germ-line cells, and that such ignorance constitutes a moral argument against intervention. The risks are unknown and incalculable.

Since that time, of course, a lot has happened, including the possibility of 'therapeutic cloning ' of human tissue. But at the time, her certainties gave many non-scientists security. It is for this, as well as for her spellbinding powers of exposition and explanation that I want to record my deep gratitude.