Looking more closely at the A (assistance) and the T (technology) in Assisted Reproductive Technology (ART)

Working paper

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French law presently restricts access to assisted reproductive technology (ART) to persons defined as needing some form of medical attention; however, ART is not strictly speaking a cure for infertility or for whatever malady justifies its use. Rather, it is a form of palliative medicine, meaning that it offers an alternative form of medical treatment to the person it cannot cure. A palliative approach to illness is more widespread than we may think, and includes not only palliative care at the end of life, but also prosthetics and transplantation. Reproductive technology, thus understood, is simply an alternative method to heterosexual relations for conceiving children. As such, ART becomes an option for persons who are not in heterosexual relationships, and who nonetheless wish to have children.

In France, where the law implicitly rejects such as an option as illegal, access by single women, persons in same-sex relationships and persons who identify as transgender has been the object of heated discussions. In this context, crucial issues related to the technology itself and to the fact that most require medical intervention, have been sidelined, if not ignored. Reproductive technology has tended to be viewed as fundamentally beneficial, or at least as value-neutral, with a presumption that more access and more technology implies more choice and better health. Yet many of these procedures involve some risk to health, and genetic screening and diagnostic techniques that, associated with ART, may reduce the risk of serious disease in offspring, also call to mind past issues in eugenics as well as newer issues related to human enhancement. If reproductive technology has opened new pathways in family formation, it has above all changed our expectations and experience of reproduction, our views about what is acceptable in terms of reproductive risk-taking and about what we expect in terms of health care and health improvement.
To better understand what ART is and has to offer, we need to take a closer look at ART’s scientific history and the scientific and technological imaginary that underlies it. In my presentation, I will briefly examine three changes in our reproductive practices brought about by ART: the separation of reproduction from heterosexual relations; the transfer of fertilization from women’s bodies to the laboratory; and the externalization and cryopreservation of reproductive cells and fertilized embryos. These three changes have radically altered the conditions under which children are conceived: they have increased the number and the types of persons (physicians, biologists, prospective parents, donors,…) involved in conception; and they have broken down fertilization into distinct phases that can be extended in time and in space (notably through cryopreservation and storage of reproductive materials). This has multiplied the situations in which disagreements may arise, creating potential for conflict among the numerous protagonists.

ART cannot be reduced to a twentieth-century technical revolution. Its history begins in the 18th century, when the scientific approach to the investigation of nature was undergoing a sea change. Describing natural processes was no longer to be based exclusively on the detailed observation and comparison of these processes, but on the attempt to “imitate nature”, that is, to reproduce them in the laboratory using technical devices. This was the beginning of experimental biology, a specialty in which the Italian abbot and biologist Lazzaro Spallanzani (1729-1799), occupies a prominent place. Involved in the heated scientific discussions on the origins of the individual organism (do embryos come from egg or sperm?), he conducted a series of experiments on animal reproduction that perfectly illustrates this approach. One of these experiments involved the artificial insemination of a dog. He concluded from his studies that contact between both egg and sperm is necessary for an individual organism to develop, but this contact is also sufficient; in other words, fertilization without sexual intercourse can be produced simply by "imitating nature". Spallanzani’s experiments marked the beginning of the realization that reproduction could be separated from sexuality.

This revolution in the way of thinking about fertilization was rapidly adopted by physicians. In France, the title of a book written on artificial insemination by Michel Augustin Thouret, Dean of the Faculty of Medicine in Paris - *Application to the human species of the experiments carried out by Spallanzani on a few animals, relating to the artificial fertilisation of germ cells, or the result of an experiment which proves that children can be created with the help of both sexes but without their approach* (Paris, 1803) - explicitly
attests to this practice. Artificial insemination is used discreetly in medical practice to circumvent various obstacles, mostly male, to fertilization: genital malformations (such as the hypospadias, a congenital disorder of the urethra that motivated the first case allegedly treated by the Scottish surgeon John Hunter in 1790), or sexual dysfunction. Several sealed envelopes deposited at the French Academy of Medicine by 19th century physicians, subsequently opened and analyzed in the late 20th century by the French physician and biologist Georges David (1987), also give us a glimpse of other indications, some of which had no medical justification whatsoever (e.g. aversion to sexual relations with the wife). This practice developed despite a lack of knowledge about how conception occurs (understood only around the 1850s) or at what time in a woman’s cycle ovulation occurs (established in 1923 by Kiusaku Ogino in Japan and Emil Knauss in Austria – research that was the basis for what is called the “rhythm method”). The practice of artificial insemination was shrouded in secrecy, even when the practice involved only the husband’s sperm, mostly because it was considered not only medically illicit but also immoral for a physician to interfere directly with reproduction – what 18th century biologists would have called “imitating nature”. The first attempts to use donor sperm towards the end of the 19th century only aggravated the hostile climate surrounding ART and reinforced the clandestine nature of the practice.

The development of the second change brought about by ART – the externalization of the fertilization process – has its roots in the early twentieth century. Robert Edwards and Patrick Steptoe are rightly credited with the development of in vitro fertilization (IVF) and the birth in 1978 of the first child, Louise Brown, conceived using this method. However, if Robert Edwards spent years carrying out much of the experimental groundwork on the biology of fertilization, he was not the first to do so. Gregory Pincus, best known for his role in the development of oral contraception, was one of the first experimental biologists to do research on mammalian ova and to examine the conditions of their maturation and fertilization, in vivo and in vitro (1935, 1936). Indeed, Robert Edwards claimed that Pincus was “a great hero of mine” (Reproductive Biomedicine Online, 2005, p. 2). Even Pincus’ work was inspired by pioneering research on the parthenogenesis of sea urchins done in the early 1900 by the German-American biologist Jacques Loeb. Both Pincus and Edwards were hindered in their work on reproductive biology, notably through loss of financial support, because of moral objections to the type of manipulations involved, the material used - human reproductive cells and embryos – and the risk of future application on humans. Moreover, when Edwards began studying the fertilization of human ova, few physicians accepted to
provide him with pieces of excised ovarian tissue from which he could cull immature oocytes. Most physicians found his request “preposterous” (*Nature Medicine*, 2001).

Whereas Pincus decided to reorient his work towards the hormonal regulation of fertilization, Edwards chose to deal openly and directly with these objections, finding when necessary private support for his research. He persisted in his project, counterbalancing the slow moments in his study of fertilization with other projects oriented towards the study of embryo development, the derivation of embryonic stem cell lines from the inner cell mass, and the premises of preimplantation genetic diagnosis (sexing of embryos). Ultimately, he found an eager collaborator in the gynecologist Patrick Steptoe, who had developed a technique known as laparoscopy that made it possible to aspirate oocytes directly from the follicles in women’s ovaries. Together they advanced on IVF as a form of infertility treatment.

Artificial insemination was a technique simple enough to be adopted outright by physicians for their own practice. Developing IVF, however, required cooperation between biologists and physicians, both during the experimental laboratory stage (to provide the biologist with the human biological material necessary for his studies), and later during its clinical implementation (to obtain the gametes necessary for fertilization and then to transfer the resulting embryo into the uterus). This creates a situation in which the medical application of a new technique is never totally dissociated from the research projects from which it has evolved and which it continues to nourish. This tension between two distinct objectives – research and therapy – is illustrated by the fact that, once IVF was recognized as a valid medical procedure, one of Edwards’ publications (with A. Fishel and C. Evans in *Science* 1984) was criticized because not all embryos fertilized in the context of IVF were being used for patient treatment. This ultimately led to a change in policy at their clinic, Bourn Hall, and elsewhere, requiring informed consent for embryo donation to research.

The diversification of ART research and practice has been in part dependent on another of its technical aspects, the cryopreservation of reproductive cells and embryos. This also has a long history. Spallanzani was one of the first to have observed (with the aid of a microscope) that viable sperm could be found in a previously frozen semen sample. Paolo Mantegazza, a 19th century Italian physician and anthropologist who studied, among other things, reproductive and sexual medicine, conducted similar experiments on the effects of freezing on sperm. Indeed, he was one of the first to suggest the creation of semen banks for men, especially soldiers, who wished to ensure the future impregnation of their wives in case
of death. However, semen banks did not become feasible until the second half of the 20th century when glycerol, a cryoprotective agent, was discovered in 1949, and a slow freezing technique with liquid nitrogen was developed in 1964. Used together, they could ensure good fertilizing capacity after thawing. The same technique turned out to be useful for cryopreserving embryos, but not for the freezing of oocytes whose high fluid content required the development of a specific technique, called vitrification. At present, all reproductive cells and embryos can be frozen and stored, either for personal use in conceiving children or for research purposes.

The ongoing connection of ART with research on contraception is also enlightening when we consider the proposal made by another pioneer of oral contraception, the biochemist Carl Djerassi. In a paper published in *Nature* in 1994 on male contraception, Djerassi lamented the lack of progress in this field and suggested as the only viable alternative, vasectomy following the cryopreservation of semen, with artificial insemination as the means to produce pregnancy. “Until now, human birth control has been achieved by interfering in the reproductive cycle of the fertile person. In the future….the ‘normal’ reproductive state of an adult may be infertility, a subsequent deliberate step being needed for fertilization.” (*Nature* 1994, p. 12) In the last twenty years before his death, he began publishing abundantly around the leitmotif: are sex and fertilization ready for a divorce? This proposal detaches ART from the idea that one should have a medical reason for access; but it nonetheless transforms reproduction into a medical-organized procedure. Whereas this idea may have seemed “preposterous” in 1994 to those who first read it in a scientific journal, it may now appear less so in a context where medically assisted reproduction has become commonplace, and where both women and men are being encouraged to cryopreserve their gametes for future use. The routine use of ART rather than sex to conceive one’s children may also make sense if one wishes to reduce reproductive risk through the genetic screening of reproductive partners and of future offspring.

Looking at how science and medicine have collaborated over the years to produce innovative procedures that offer a novel approach to age-old problems may also give us a clue as to the aspects of this technology which we may not wish to buy with it – if that is at all possible. Ultimately the development of ART raise questions as to how much control over reproductive matters and materials individuals wish to share with health care professionals and institutions, to what extent this reproductive partnership is based (or not) on shared values, and who will ultimately make the important decisions.
References


Thouret, Michel Augustin. Application sur l'espèce humaine des expériences faites par Spallanzani sur quelques animaux, relativement à la fécondation artificielle des femmes ou résultats d'une expérience qui prouve que l'on peut créer des enfants avec le concours des deux sexes mais sans leur approche. Paris, Charles Pougens,1803.