

## Sex and Fertilization: Ready for Divorce?

With very few exceptions, the millions of different species on this earth—from insects and reptiles to fish, birds and mammals—copulate in order to procreate. What we create in that act is not primarily an extension of ourselves, however; it is an extension of the species merely. What strives for genetic immortality is not the individual—that ambition remains beyond our grasp—but the genome. This general set of chromosomes, rather than the particular combination of brown hair and hazel eyes, musical talent and athletic ineptitude, is the ultimate beneficiary of all that sweat and struggle in the dark. It carries no personal stamp of knowledge. With few exceptions, most males other than humans do not actually know who their offspring are, nor do the fathers of most species have anything to do with the upbringing of the next generation.

Not so with man. Parenthood is driven largely by a deep, personal association with one's children, indeed by obsessive identification with them. It takes little imagination to relate the desire for parenthood to a desire for a form of immortality, even at such simple a level as perpetuation of one's family name. Once we recognize this equation, many of the traditional attempts at regulating sexuality take on a new significance. Until recently, becoming a biological parent invariably meant achieving successful fertilization of a woman's egg by a man's sperm through sexual intercourse. Many religions, Catholicism being a prime example, insist that sexual intercourse not only be monogamous, thus clearly defining the biological identity of the offspring, but also that it be sanctioned only if reproduction is its formal objective. Judaism, on the other hand, through its reference to the mother rather than father for purposes of identification, tacitly acknowledges the uncertainty of paternal credentials. But these attempts at confirming the identity of the offspring are not all that seems to govern our traditional sexual mores: it does not so neatly explain, for instance, the Catholic Church's disapproval of contraception, which seems at times reducible to the injunction, "You must not have sex just for fun."

Yet denying the overriding influence of the pleasurable aspects of sex is illogical. The Church is not against "natural family planning," against sexual intercourse during the time of a woman's menstrual cycle when she is infertile because she has already ovulated or has not yet started to ovulate. The injunction would then seem to be something subtler, along the lines of, "You cannot have sex just for fun, unless there is some element of risk." It was primarily the uncertainty of accurately predicting the infertile days in a woman's monthly cycle that made such "natural family planning" into "Vatican roulette". But now, as new biochemical techniques enter the market that permit women to determine with near-perfect certainty whether they are in a fertile period of their menstrual cycle, such "hormonally-based natural family planning" just becomes another form of deliberate birth control. (I have become so interested in that topic that it even became one of the themes of my latest science-in-fiction novel, *NO*). Why has the church so far not prohibited it? Is it because its relatively high failure rate is not due to the inherent uncertainty of such hormonal tests, but rather to human frailty - the lack of sexual discipline of the couples in refraining from intravaginal intercourse during the "unsafe" period of the menstrual cycle?

There are other interesting religious exceptions to the ostensibly exclusive reproductive function of sexual intercourse. Among Orthodox Jews, sexual relations are not

permitted during menstruation or when even the slightest evidence of spotting is observed. But there are women, who show occasional spotting during mid-cycle and during ovulation—in other words women who are not permitted to copulate precisely during their fertile period because the odd drop of blood can still be observed on a white sheet. Such couples are not infertile, but clearly they will not become parents through ordinary intercourse. (This prohibition of intercourse during bleeding, of course, has less to do with subordinating sexual pleasure to reproduction than it has to do with rituals of taboo/abjection/misogyny).

Or take the man whose sperm count is 1–3 million sperm rather than the usual 50–150 million sperm per ejaculation. A couple of million sperm sounds like a lot of sperm, but they are insufficient to effect normal fertilization. Such men are diagnosed as suffering from severe oligospermia and are functionally infertile. But it is now possible to fertilize a woman's egg with the sperm of her functionally infertile husband by various forms of artificial insemination, provided his sperm is first collected in a condom—a procedure totally forbidden to observant, Orthodox Jews. *"Thou shalt not spill thy seed"*—an elegantly worded prohibition against masturbation—is the source of the Orthodox Jewish disapproval of condoms. Yet the Jewish religion, like most others, favors procreation, and a modern chief rabbi in Israel found a compromise that seemed Solomonic in its wisdom. He punctured a condom with a pin, so that a small amount of semen could leak through the minute opening, thus claiming the theoretical possibility of fertilization while retaining 90% or more of the semen for subsequent artificial insemination techniques.

But whatever the uncertainties and inconsistencies that may arise as a result of the uneasy relationship between ancient religion and contemporary science, the overall pattern remains clear enough. In emphasizing reproduction over sexuality, in assuring that the offspring actually does convey the parents' genetic material into another generation, religion is simply serving one of its central functions—the promise of immortality. But must this genetic function be related to sex? Some of the most startling developments in contemporary science, and the social changes that accompany them, have started to shatter the historically unquestioned connection between sex and reproduction. The ultimate consequences of such separation will be profound, and not the least of them will be our ability to control the very nature of our immortality.

But to reach that exalted end, we must start on somewhat lower ground, and observe that man is the sexiest of all species on earth. Among the millions of species, only we have sex for fun. Only we—and perhaps a couple of others such as the Pygmy Chimp (Bonobo)—are able and willing to have sex 365 days of the year. In all other species, copulation is seasonally controlled, and directly related to the optimal time for fertilization and the rearing of offspring. According to some reproductive biologists, such as Roger V. Short, the fact that man is the sexiest animal on earth is responsible for the extraordinary size (in relation to body size) of a man's erect penis. Compare it to that, say, of a gorilla, which is at best the size of a human thumb. Why should we need such an absurdly thick, swollen object to deliver sperm into a woman's vagina—ostensibly the only biologically significant, *reproductive* function of a penis? Clearly, we do not. A very thin, pipette-like structure would do equally well, if not better. Roger Short argues that the thick, massive penis produces more pleasure in the female partner, who is likely to prefer such men—better equipped for pleasure—as mates. Evolutionary selection, therefore, favored men with larger, thicker penises. If that argument is valid, one might reach the conclusion that sexual pleasure in the female becomes one of the determinants of selection, and that pleasure rather than fertility comes to determine female receptivity, which then determines the frequency/timing of human sexual behavior.

But you needn't take my word for it, not when there are so many numbers that make the case more powerfully than words ever could. According to the World Health Organization (WHO), *every 24 hours* there occur over 100 million acts of sexual intercourse resulting in approximately one million conceptions, of which 50% are unplanned and 25% unwanted. It is this last estimate—250,000 *unwanted* conceptions a day—that is responsible for the occurrence every 24 hours of approximately 150,000 abortions, of which 50,000 are illegal, leading to the deaths each day of 500 women. What these figures do not say is how much effort has gone into avoiding conception before the fact, nor do they tell the tale of unwanted intercourse, or intercourse occurring under the influence of alcohol or other drugs. But even without those numbers, it is clear that something in addition to reproduction is driving all this. If a quarter of the conceptions that do occur are unwanted (unwanted even in the face of an ideology that so clearly favors reproduction), so unwanted that women risk legal sanction, even death, to end them fully 60% of the time, then clearly a significant percentage of these 100 million daily coital acts has little to do with reproduction or any desire to perpetuate the species. The *possibility* of indulging in sex without reproductive consequences through the widespread use of deliberate birth control is less than 100 years old (although history records plenty of recipes promoted to accomplish that aim). The true *realization* of “sex for fun” occurred only about forty years ago with the introduction of the Pill and of IUDs (intrauterine devices) that for the first time totally separated the coital act from contraception. Women who used these were temporarily sterile, and thus could indulge in sexual pleasure without the fear of an unintended pregnancy. Clearly, all of the millions and millions of couples indulging in such intercourse did so without any desire for reproductive immortality. In principle, for millions of couples, the decision to reproduce became a deliberate choice rather than a form of reproductive gambling. But to achieve a total separation of sex and fertilization requires two components. The first is effective contraception—the virtual guarantee of not creating new life during sexual intercourse. But this by itself does not permit a complete uncoupling of sex and fertility; to reproduce, one must still couple. Until recently, that is. The second component is the extreme counterpart of the first—to create new life *without* sexual intercourse. Our species achieved this capability in 1978 in England, through the birth of Louise Joy Brown. Louise was conceived under a microscope, where her mother's egg was fertilized with her father's sperm; the fertilized egg was reintroduced into the mother's womb two days later, and, after an otherwise conventional pregnancy, a normal girl baby was born nine months later. This technique has since become widely known as *in vitro* fertilization (IVF)—an event that has now been replicated at least 300,000 times through the birth of that many IVF babies.

When Steptoe and Edwards developed IVF in 1977 they did not set out deliberately to make possible the separation of sex from fertilization. They, as well as other clinicians, were focused on the treatment of infertility. Infertility is itself an ethically charged topic. To put it bluntly and brutally, why should one treat infertility? From a *global* perspective, there are too many fertile parents, hence there are too many children, many of whom no one wants. The course of world history will not change if no case of infertility is ever treated, but it will change dramatically if excess human fertility is not curbed. From a *personal* perspective, however, the drive for successful parenthood is often overwhelming. Infertile couples are prepared to undergo enormous sacrifices, financially, psychologically as well as physically, to produce a live child under conditions where nature has made it impossible. The question may well be asked whether the realization of parenthood by biologically infertile couples carries some ethical imperative—for or against.

The enormous ethical dimensions of the problem become somewhat easier to see if we consider the question of male infertility. This issue was addressed in 1992, when a group of investigators (Palermo, Joris, Devroey, and van Steirteghem) in Belgium published a sensational paper announcing the birth of a normal baby boy fathered by a man with severe oligospermia (insufficient number of sperm). This child was made possible through the invention of an IVF technique called “ICSI,” for “intracytoplasmic sperm injection,” in which a single sperm under the microscope is injected directly into a human egg. Whereas in the original English IVF work, the egg was flooded with millions of sperm (as in ordinary sexual intercourse), with ICSI the artificial insemination was accomplished with one single sperm. The technology that makes such a fertilization possible also allows a radical revision of the definition of infertility. ICSI can be applied not only to men with low sperm counts, but to men who have *no mature sperm whatsoever*.

Such men suffer from an inherited condition of total infertility, called “congenital, bilateral absence of the vas deferens.” The vas deferens is the duct connecting the testis to the urethra, and is the organ where sperm is stored and then transported to the urethra and expelled during ejaculation. Without the vas, there is no sperm available for fertilizing an egg; clearly a man with such a condition can never become a father through sexual intercourse. But note that the barrier to fertility in such a case is not absolute—even immature sperm possess all the genetic material necessary to pass on a man’s genetic heritage to posterity. It is the machinery of mobility, and the enzymes that penetrate the egg’s cell wall, that are lacking because they are acquired during maturation. With ICSI, however, the machinery of the laboratory can supply whatever the sperm lacks. One can even aspirate immature sperm directly from the testis and inject its DNA into an egg under the microscope. Such fertilizations have been accomplished, and numerous such men have now become successful fathers! Is this acceptable? Does such an infertile man have the right to *demand* that such reproductive technology be made available to him? And does it matter what motivates such a demand? Does it make a difference if we imagine we are settling the ultimate fate of a child—a concerned party, certainly, but one whose concerns cannot be said to exist except as a consequence of our decision? Or if we are simply satisfying a person’s desire to achieve immortality? And how does it change that question if we consider what we are actually doing here—making the uninheritable (i.e. genetic infertility) heritable?

This turns out to be more than an ethical quibble. In one case out of four, men with “congenital bilateral absence of the vas deferens” are also carriers of the gene for cystic fibrosis. With ICSI, one can envisage a scenario in which such men could pass on to their offspring both infertility and cystic fibrosis, raising the specter of successive generations requiring ICSI in order to perpetuate their genetic immortality—an immortality compromised by a disease that brings a slow, early death.

The first ICSI baby is only 10 years old, but in that interval over 10,000 ICSI babies have been born. I have felt that the questions this technology raises merit wider debate than the traditional venues of a journal article or academic lecture allow. That is why I have incorporated these questions first into a novel (*Menachem’s Seed*) and then into a play, entitled “*An Immaculate Misconception*”. Here is an excerpt from a scene of that play featuring a discussion between Dr. Melanie Laidlaw, a reproductive biologist and (in the play) the inventor of ICSI, and her clinical colleague, Dr. Felix Frankenthaler, whom she had invited into her laboratory. After she informed him that she is almost ready to perform the first ICSI injection into a human egg (without, however, volunteering that she will pick her own egg for such experimentation), they debate the possible implications of this work beyond simply treating male infertility:

**Melanie:** If your patients knew what I was up to in here... they'd be breaking down my door. Men with low sperm counts that can never become biological fathers in the usual way.

**Frankenthaler:** My patients just want to fertilize an egg. They won't care if it's under a microscope or in bed... as long as it's their own sperm.

**Melanie:** You're focusing on male infertility... that's your business. But do you realize what this will mean for women?

**Frankenthaler:** Of course! I treat male infertility to get women pregnant.

**Melanie:** Felix, you haven't changed. You're a first-class doctor... but I see further than you. (Pause). ICSI could become an answer to overcoming the biological clock. And if that works, it will affect many more women than there are infertile men. (Grins). I'll even become famous.

**Frankenthaler:** Sure... you'll be famous... world-famous... *if* that first ICSI fertilization is successful... and if a normal baby is born. But what's that got to do with (slightly sarcastic) "the biological clock?"

**Melanie:** Felix, in your IVF practice, it's not uncommon to freeze embryos for months and years before implanting them into a woman. Now take frozen eggs.

**Frankenthaler:** I know all about frozen eggs.... When you rethaw them, artificial insemination hardly ever works.... Do you want to hear the reasons for those failures?

**Melanie:** Who cares? What I'm doing isn't *ordinary* artificial insemination ... exposing the egg to lots of sperm and then letting them struggle on their own through the egg's natural barrier. (Pause). We inject right *into* the egg... Now, if ICSI works in humans... think of those women—right now, mostly professional ones—who postpone childbearing to their late thirties or even early forties. By then, the quality of *their* eggs... *their own* eggs... is not what it was when they were ten years younger. But with ICSI, such women could draw on a bank account of their frozen *young* eggs and have a much better chance of having a normal pregnancy later on in life. I'm not talking about surrogate eggs—

**Frankenthaler:** Later in life? Past the menopause?

**Melanie:** You convert men in their fifties into successful donors—

**Frankenthaler:** Then why not women? Are you serious?

**Melanie:** I see no reason why women shouldn't have that option... at least under some circumstances.

**Frankenthaler:** Well—if that works... you won't just become famous... you'll be notorious.

**Melanie:** Think beyond that... to a wider vision of ICSI. I'm sure the day will come—maybe in another thirty years or even earlier—when sex and fertilization will be separate. Sex will be for love or lust—

**Frankenthaler:** And reproduction under the microscope?

**Melanie:** And why not?

**Frankenthaler:** Reducing men to providers of a single sperm?

**Melanie:** What's wrong with that... emphasizing quality rather than quantity? I'm not talking of test tube babies or genetic manipulation. And I'm certainly not promoting ovarian promiscuity, trying *different* men's sperm for each egg.

**Frankenthaler:** "Ovarian promiscuity!" That's a new one. But then what?

**Melanie:** Each embryo will be screened genetically before the best one is transferred back into the woman's uterus. All we'll be doing is improving the odds over Nature's roll of the dice. Before you know it, the 21st century will be called "The Century of Art."

**Frankenthaler:** Not science? Or technology?

**Melanie:** The science of... A... R... T (Pause): assisted reproductive technologies. Young men and women will open reproductive bank accounts full of frozen sperm and eggs. And when they want a baby, they'll go to the bank to check out what they need.

**Frankenthaler:** And once they have such a bank account... get sterilized?

**Melanie:** Exactly. If my prediction is on target, contraception will become superfluous.

**Frankenthaler:** (*Ironic*) I see. And the pill will end up in a museum... of 20th century ART?

**Melanie:** Of course it won't happen overnight.... But A... R... T is pushing us that way... and I'm not saying it's all for the good. It will first happen among the most affluent people... and certainly not all over the world. At the outset, I suspect it will be right here... in the States... and especially in California.

**Frankenthaler:** (*Shakes head*) The Laidlaw Brave New World. (*Beat*). Before you know it, single women in that world may well be tempted to use ICSI to become the Amazons of the 21st century.

**Melanie:** Forget about the Amazons! Instead, think of women who haven't found the right partner... or had been stuck with a lousy guy... or women who just want a child before it's too late...in other words, Felix, think of women like me.

ICSI raises many other ethical and social problems beyond those mentioned in the Melanie/Felix dialog. For example, now that the effective separation of Y- and X- chromosome-bearing sperm has been perfected, ICSI will enable parents to choose the sex of their offspring with 100% certainty. For a couple with three or four daughters, who keep on breeding in order to have a son, the ability to choose a child's sex may actually prove a benefit to society, but what if practiced widely in cultures (such as China or India) that greatly favor male children over girls?

Or consider the capability of preserving the sperm of a recently deceased man (say 24–30 hours post mortem) in order to produce (through ICSI) a live child months or even years later—a feat that has already been accomplished. Here we have immortality with a vengeance. But what of the product of such a technological tour de force? Using the frozen sperm and egg of deceased parents would generate instant orphans under the microscope. The prospect is grotesque—yet does it take much imagination or compassion to conceive of circumstances where a widow might use the sperm of a beloved deceased husband so that she can have their only child? These issues are intrinsically gray; the technology occupies an ambiguous position, enabling us to enact our best and worst impulses, and the answers cannot be provided by scientists or technologists. The ultimate judgment must be society's, which, in the case of sex and reproduction, really means the individual affected. Ultimately, that individual is the child, yet the decision must be made before its birth by the parents—or more often than we care to admit, by just one parent.

It is the nature of such questions that they resist convenient solutions, not least because of their tendency to proliferate faster than we can solve them. Whereas reproduction has historically tended to exemplify the law of unintended consequences, the addition of technology has given that law added force. Consider: until very recently, the onset of the menopause was welcomed by many women as the release from continuous pregnancies caused by unprotected and frequently unwanted intercourse. But the arrival of the Pill and other effective contraceptives, coupled with the greatly increased number of women entering demanding professions that cause them to delay childbirth until their late thirties or early forties, now raises the concern that the

menopause may prevent them from becoming mothers altogether. Whereas reproductive technology's focus during the latter half of the 20th century was *contraception*, the technological challenge of the new millennium may well be *conception* (or *infection*, if one focuses on sexually transmitted diseases). In the long run, if the cryopreservation of gametes followed by sterilization becomes a common practice, contraception may even become superfluous. Melanie and Felix in the above fictitious dialog were hardly the first to express such speculation.

In 1994, in the scientific journal *Nature*, the cryobiologist Stanley Leibo and I addressed the deplorable prognosis for a new male contraceptive in the next few decades, given the total lack of interest in that field by the large pharmaceutical companies without whose participation such a "Pill for Men" could never be introduced. This led us to propose an alternative approach, not involving the drug industry, based on a few simple assumptions.

Millions of men—admittedly, most of them middle-aged fathers rather than young men—have resorted to sterilization (vasectomy) and continue to do so. The procedure is much simpler and less invasive than tubal ligation in women. (Sterilization among both sexes has become so prevalent that in the U.S., it is now the most common method of birth control among married couples, even surpassing the Pill). Artificial insemination is both simple and cheap. Furthermore, among fertile couples, it has almost the same success rate as ordinary sexual intercourse. But most important for our argument, fertile male sperm has already been preserved inexpensively for years at liquid nitrogen temperatures. Therefore, provided one first demonstrated that such storage is possible for several decades rather than just years, some young men might well consider early vasectomy, coupled with cryopreservation of their fertile sperm and subsequent artificial insemination, as a viable alternative to effective birth control. Shifting more of that responsibility to men, at least in monogamous, trusting relationships, appeared to Leibo and me a socially responsible suggestion. I shall spare the readers a record of the resulting outcry—both by media and in personal correspondence—but a lot has happened in the intervening few years to make it much more likely that such a prediction will become fact within a few decades rather than dramatic license.

Although many may consider some of the scenarios raised in *An Immaculate Conception* as "unnatural" or worse, every one of them has now been realized or is about to be implemented. Take the question of post-menopausal pregnancies. In progressively more geriatric societies (for example, in Japan or Western Europe), where 20 per cent of the population is already or will soon be over the age of sixty, and older people are increasingly healthier than they used to be, a woman who becomes a mother at 45 could raise a child for a considerably longer time than could a 20-year-old at the beginning of this century. Of course, motherhood at an older age is physically, psychologically, and economically suitable only for certain women, but at least the choice is now available in wealthy countries. It must be emphasized that this increased emphasis on artificial fertilization techniques and even surrogate parenthood is a characteristic of the affluent, "geriatric" countries. Even within these countries, the cost of such reproductive technologies (frequently not covered by insurance) is such that only the more affluent citizens can afford them. Three-fourths of the world's population are represented by the "pediatric" countries of Africa, Asia and much of Latin America, where over 40% of the population may be below the age of fifteen and where the control of fertility rather than the treatment of infertility will remain the catchword for decades to come.

I have deliberately refrained from considering the implications of human cloning—the closest technological approach to immortality. But to the extent that biological par-

enthood is a form of immortality—admittedly one subject to mutational and hence evolutionary adjustments—IVF tampers with that as well. In the excerpt from my play, I allude to pre-implantation embryonic genetic screening, again a procedure primarily available to the affluent in the affluent countries. But soon, the entire human genome will be elucidated. Given the many technically feasible methods of rapid genetic screening, what will keep prospective IVF parents from screening their own embryos so as to transfer only the “best” back into the mother? Who will define “best”? Few people will argue that prospective parents may wish to discard embryos that show the markers for Down’s or Huntington’s Syndrome, or markers for genetically transmitted cancers, but where will the line be drawn? Short stature? Left-handedness? Big ears? As we move in the direction of tailor-made progeny, the gulf between the haves and have-nots is widening enormously.

The recent advances in contraceptive and reproductive technologies have clearly raised a multitude of gray problems which many of us would like to wish away. But that is not possible anymore—the genie has escaped from the bottle. Legislation will not offer a solution, unless it were global in nature. Otherwise, a committed couple—or perhaps just the woman—will cross geographical borders in an attempt to circumvent biological ones. The answer is intensive and continuous debate, based on knowledge rather than myth, which is one of the reasons why I, the scientist, have moved to fiction and drama as novel ways to raise the intellectual level of public discourse of sex and reproduction.

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### Relevant literature by Carl Djerassi

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