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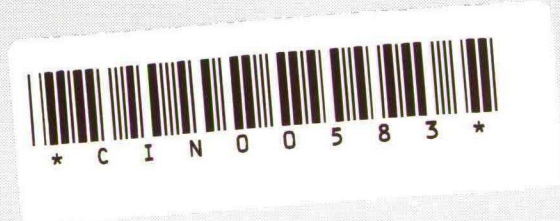
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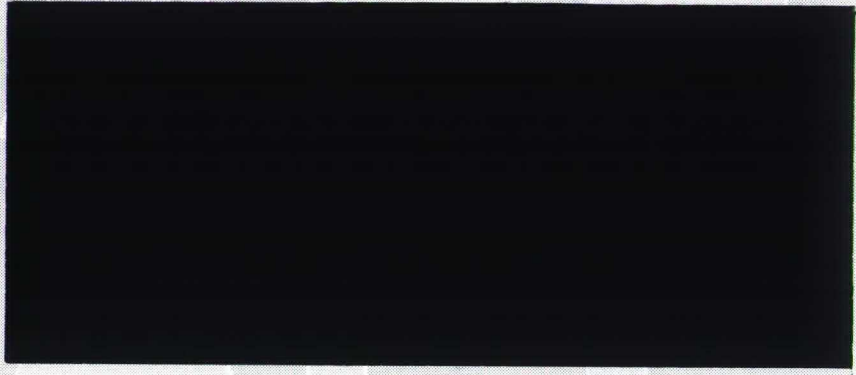
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**The Impact of Some Biomedical
Advances on Reproduction and Parenthood**

Prof.dr. E.R. te Velde

WORC PAPER 94.05.029/6

Paper prepared for the Conference on Changing Fatherhood,
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**The Impact of Some Biomedical
Advances on Reproduction and Parenthood**

Prof.dr. E.R. te Velde

Keywords: Fertility, Assisted Reproduction Techniques, Postponed Parenthood

In 1645 father Cats, the popular poet of our Golden Age, clearly described the domains where husband and wife belonged:

"The husband must be on the street to practise his trade

The wife must stay at home to be in the kitchen

The diligent practice of street wisdom may in the man be praised

But with the delicate wife, there should be quiet and steady ways

So you, industrious husband, go to earn your living

While you, oh young wife, attend to your household".

According to Pott-Buter the combination of Calvinistic doctrine and the relative wealth of the Dutch Republic in the Golden Age of the 17th century, possibly explains why the ideals of the perfect housewife and the caring mother came to shape much earlier and possibly also deeper in the Netherlands in comparison to other countries.

This ideal, unanimously cherished by protestants, catholics and socialists was at the roots of our social welfare system created in the fifties. It was translated in a complicated network of regulations, laws and allowances aiming to compensate for the highly valued work housewives were doing at home. By this system it was not necessary any more for married women to have to work outside their homes in order to provide the additional money for keeping the family going.

The fundamental changes that occurred since the sixties, primarily influenced the role and identity of women. To my mind, changing fatherhood is a secondary phenomenon. Therefore, I will mainly talk of motherhood and parenthood and rarely of fatherhood. Nevertheless, I agree that fatherhood also has dramatically changed, but this change did not come voluntarily, the woman forced him to change, generally speaking.

In the following I will focus on some biomedical advances - birthcontrol methods and techniques for assisted reproduction - which already have fundamentally changed the reproductive fate of women. Without any doubt, further changes will continue to occur in the future, may be quite soon.

Birth control methods

Oral contraceptives, the principle of which was developed by Pincus in the forties, became available in the sixties. However, only at the end of that decade a pill was constructed, the side effects of which had decreased to such a level that they became acceptable to the majority of women. At the same time many societal changes could be noticed such as postponing pregnan-

cy, permanently deciding against parenthood, increasing female labour force participation, rising female educational levels, unmarried cohabitation or living alone, increasing secularization and urbanization. The common denominator of these changes is the growing emancipation primarily of women but also of men. All of these processes gained momentum from the end of the sixties and the beginning of the seventies, at about the same time the radical change in the use of contraceptives started. In 1971 the pill was included in the National Health package, after which its use rapidly increased and it became the most popular birth control method. Around that time the number of sterilizations increased as well, first among females and later among males. Compared to other Western countries, these trends were more radical in the Netherlands. In a comparison with 37 other Western countries, the Netherlands ended up at the top of the list with respect to birth control, among other things, based on the effectiveness of contraceptive use and the low rate of induced abortions and teenage mothers. Knowledge on the use and effectiveness of the condom and the pill are standard items on a Dutch adolescent's curriculum. Information on the morning-afterpill can be requested via the children's helpline.

The widespread availability of reliable contraception, by which the link between sexuality and reproduction is broken, has undoubtedly been an important condition for the aforementioned societal trends. For most women, having children is no longer an obvious and unavoidable biological fact that a woman just has to put up with. It has become an issue for careful consideration, planning, and postponing. Currently many couples remain in doubt more often and much longer whether they do or do not want "to take" a child. The key to this doubt, which sometimes becomes an obsession, lies in the virtually impossible combination of a child with a job or studies, and in the threatened loss of personal freedom. Due to this, many women decide at younger ages not to have children at all, and some change their minds at a later age. After this decision most couples like more than one child. There is no doubt that the process

of postponement will continue and that women will have children later and later.

Although the above societal trends have been taking place in all Western countries, the developments in the Netherlands have been most radical: the Dutch are world champions at birth control and motherhood is postponed longer than in any other country of the world.

If you compare the Dutch schemes and facilities with those of other European countries, it is striking how easily a pregnancy can be prevented or terminated, and how difficult it is to combine motherhood with a job. I like to briefly mention few of the Dutch facilities. Contraceptives are inexpensive, easily accessible, and widely available. Public access to information on birth control is excellent. In contrast to this, the recently implemented parental leave scheme will only be attractive for those parents with a high income because, in addition to a drop in income, there is a risk of losing accrued pension rights. There is no adequate leave scheme when one's child is ill. Flexi-hours at work for parents who have school-aged children are not encouraged by the government. Childcare facilities for 0 to 4-year-old children are very scarce, with a demand already being 10 times higher than the current supply. The Emancipation Council expects that this will become many times higher in the near future. There is no consistent afterschool child-care after the age of four. The Netherlands is also low on the European list with respect to financial child support. It is no wonder that female labour participation in the Netherlands belong to the lowest in Europe, and that most women quit their job after they have had a baby. Why this typically Dutch discrepancy in facilities that stimulate preventing pregnancy (and consequently postponement or complete rejection of parenthood) and discourages combining motherhood and a job? Undoubtedly, it is the consequence of our social welfare system founded in the fifties and still going strong in the nineties. Times have changed and the ideal of the perfect housewife has for a great part been replaced by the ideal of the

independent and free women, who wants a professional career and earns her own money. Many of the regulations and allowances meant to realize the ideals of the fifties are very expensive. The Scientific Council for Government Policy has calculated that one of these allowances, the so-called "overdraagbare basisaftrek" which forms a barrier for a woman to start working, already costs about 4 milliard guilders per year. After it has been spent no money is left for a policy allowing for the combination of work and having children. Dutch parents are more or less forced to postpone their parenthood unless women are ready to give up work and career.

So why not postponing parenthood? One of the objections is that female fertility starts to decrease after the age of 30 and strongly after the age of 35. The considerable increase of subfertility and infertility probably is mainly due to the growing trend of postponing motherhood. It has been estimated that about one third of couples of whom the woman is 35 or older, have a fertility problem. Are they to be solved by Assisted Reproduction Techniques like in vitro fertilization? We will see.

In vitro fertilization

Five to ten years ago IVF was a popular issue in the media, but it has lost its innovative nature and has become a standard treatment for infertility. Nowadays everybody knows what is meant when a woman goes to hospital for getting a "test tube baby". I hesitate to mention the biological principles because they belong to the general knowledge of educated people like you. In short: a woman is stimulated with hormones from the pituitary gland - the so-called gonadotrophins - which cause the ovaries to develop many ova, instead of the one ovum that comes free during a natural cycle. We call this "controlled hyperstimulation". When the ova are

considered to be ripe, they are extracted by a syringe. In the laboratory, the partner's sperm is added in order to fertilize the ova. A number of fertilized ova, now called embryo's, are put into the uterus a few days later and thereafter we all hope that one of them implants and further develops. The object for a couple is of course not that the woman gets pregnant, but that she gets a healthy baby.

About 15% of IVF attempts results in the birth of a healthy child. If a women gets 3 attempts she has a chance of about 40% to get a baby. The average number of attempts per woman is about 2.5 with a range of 1 - 25. It is quite rare for a woman to get more than 6 attempts. During the early days, tubal pathology e.g. blocked tubes, was thought to be the only indication for IVF but since a long time all forms of infertility are treated with IVF, unless the quality of the sperm is extremely poor.

In the Netherlands, all 8 university hospitals and 4 other hospitals received permits to utilize the IVF procedure. Since February 1990, three treatments are reimbursed by the National Health and by some private medical insurance companies. In 1987 the demand of the number of IVF attempts was estimated to be 4500/year. In 1990, 6000 IVF treatments were performed and in 1992 almost 9000 resulting in about 1350 deliveries and 1800 babies. Another, extensively used assisted reproductive technique has emerged from IVF, the so-called IUI (intrauterine insemination) which is almost always combined with controlled hyperstimulation. In the IUI treatment protocol, the hyperstimulation phase is basically similar to IVF, that is, many ova are developed here as well. Immediately prior to an expected ovulation, a sample of the most motile sperm is selected in the lab. These are inserted into the uterus. The idea behind this treatment is that the probability of a sperm fertilization an ovum is increased if there is more than one ovum. This probability is further increased by inserting the "best" sperm into

the uterus closer to the ova.

As the IVF treatment is concentrated in those twelve hospitals, there is considerable data on the number of treatments and the success rate of IVF. However, little is known about the controlled hyperstimulation and IUI. This is due to the fact that this treatment can be used by every gynaecologist, and there is no permit required for making sperm samples suitable for insemination. It is quite likely that this treatment is being used on a wide scale. Based on the sales figures of gonadotropins, we calculated that in the year 1990 in the Netherlands there had been more hyperstimulation/IUI treatments, than IVF treatments. We estimate that of the almost 200.000 babies born in 1993, 3000 - 4000 are the result of assisted reproduction. So, almost 2%.

There are two relatively frequent complications - one for the woman and one for the child - associated with both methods, IVF and hyperstimulation with IUI. The term "controlled hyperstimulation" suggests that we have a good grip on stimulating the ovaries. In most cases this is true, but sometimes stimulation is more intense than expected. The ovaries become overstimulated and can become gigantic. This may result in a life-threatening situation for one percent of the women. The complications for the child are mainly determined by the highly increased probability of a multiple pregnancy and thus to premature birth. The success rate of IVF is considerably higher if more than one embryo is inserted into the uterus, but the chance of a multiple pregnancy also increases proportionally. If IVF leads to a birth, the probability of twins is twenty-five percent, and of triplets, quadruplets, or more is about 5%. However, the number of multiple births after IVF cannot by far explain the total rise in multiple pregnancies since 1980. Probably a considerable proportion of the rise in multiple births must therefore be attributed to a rise in the use of hyperstimulation in combination with IUI. Children

of a multiple pregnancy are usually born prematurely. Their only chance of survival is an intensive, technical, and lengthy treatment on so-called Neonatal Intensive Care Unit. If these children are kept alive, the probability of physical and mental handicaps in the longterm is much higher than that of children who are born on time. Parents of multiple births are exposed to more stress than parents of a single child, with mothers being particularly susceptible to depression. Especially fathers are inclined to leave home permanently. The divorce rate of parents with twins or triplets is much higher than in the normal population.

Recently, some reports have indicated that the chance of getting ovarian cancer might be increased after the use of gonadotropins or other fertility drugs. Although, these reports are far from conclusive, they do cause concern.

Influenced by the overwhelming attention by the media, assisted reproduction nevertheless has received the golden award of biomedical progress in the mind of millions of people.

In addition, to birth control methods, assisted reproduction is a further step in the feasibility of planning parenthood. This fits in the progressively growing trend in our society of calculating and planning life from the cradle to the grave. However, with regard to assisted reproduction, reality is less brilliant than its appearance. Apart from the disadvantages already mentioned, the so-called take-home baby rate of IVF sharply decreases after the age of 35 becoming almost zero after 40. We estimated that if the trend of delaying motherhood continues at the same rate, infertility because of ageing will almost triple in the year 2005 as compared to 1990. The notion of the public that motherhood can be safely postponed in this era of assisted reproduction is illusive.

Insemination with donorsperm

Insemination with donorsperm actually does not belong to modern assisted reproduction techniques because it is simple and has already been practised for decades; since the sixties in The Netherlands. I mention it because it creates unusual types of fatherhoods, whether or not the donor remains anonymous. My impression is that neither the fatherhood of the social father nor the childhood of a child born after insemination of anonymous sperm are at risk. Whether anonymity should be abolished, is a discussion I will not go into, although I secretly think "not yet please".

Intra-Cytoplasmatic Sperm Injection (ICSI)

ICSI is an exciting technique by which it is possible to inject one single sperm in one ovum. By this development men with extremely poor sperm qualities can father their own child. Until now, donor insemination was the only alternative for such men. Approximately 250 children have been born now and fortunately the chance of congenital malformations does not seem to be increased. Some experts in the field predict that ICSI may entirely replace the classic IVF, for all indications because fertilization rates may prove to be superior. ICSI has not been used in The Netherlands yet, but the first treatment will take place next week in Utrecht. I cannot think of any reason why it would influence parenthood in a different way than IVF.

Pre-implantation diagnosis (PID)

PID is already applied in some centres for a limited number of indications, but not yet in The Netherlands. Although many technical problems have still to be solved, it offers the potential of diagnosing a genetic abnormality in one single cell of an embryo. If the cell appears to be free of a genetic defect, the remaining part of the embryo can be replaced as usual because the techniques used for genetic analysis are slightly modified from those normally used for prenatal diagnosis. In contrast to the last, however, no abortion is necessary if an abnormality is found. An induced abortion of a deeply wanted pregnancy is a terrible intervention not only for the woman, but possibly also for the fetus. If the technique of PID will become easier, and it probably will within 10 - 20 years, the threshold of doing it, might become lower than prenatal diagnosis. If so, it might be used for less serious indications, for example for diagnosing the sex of the embryo if a boy or a girl is desired, or minor defects. It is also conceivable that it signifies a step in the direction of trying to create the perfect race.

The use of oocytes obtained from young women

The results of IVF indicate that it is mainly the quality of the ovum that determines the probability of pregnancy with the condition of the uterus playing only a minor role. Moreover, the quality of the ovum appears to be highly related to the age of the woman. By using ova from a young donor it is possible to obtain surprisingly good pregnancy results in women who have no functioning ovaries, also in women - as you all know - during or after the menopause. Although experience is still fragmentary, there is no reason to assume that the vascular system of healthy and active women of 50 or 60 could not endure the burden of a pregnancy. Some

psychologists point out that parents at this age are emotionally more stable and financially more secure. They are still young enough to rear and supervise their children until adolescence. At present, having children after 50 is only reserved for the happy few - financially spoken, because it is difficult and expensive to find suitable donors. However, this may change in the future when it will become feasible to freeze and store ova. At present, freezing of ova in such a way that their quality is maintained after thawing is still a technical problem, but experts predict that this solution will be available within ten years. If so, a young woman of 20 - 25 years could get a large supply of her own ova. In the future this might become possible without dangerous and time-consuming hyperstimulation procedures, by extracting a few hundred ova from a small piece of one of the ovaries. Deep freezing embryos is already possible but the disadvantage is that a partner is required for fertilizing the ova. Even for those who have already a partner at that age, it will become less and less likely that the same partner will still be around thirty years later. Therefore, a woman prefers to use her own ova. Subsequently, the woman gets sterilized, so that she will definitely be rid of all the side effects that will still be associated with contraceptives in the next century. She will not be encumbered with motherhood until after her fiftieth or perhaps sixtieth birthday, She will have the same opportunities as a man with respect to job, career, salary, recreation, sex and social relationships. Meanwhile her ova remain stored in the freezer at a temperature of minus 198° C. She can still decide not to use them, and either have them destroyed or donate them to another woman. She may also prefer to get them fertilized by a man who is both the right type to be the father of her children and the partner sharing the last decades of life. After congenital defects of the embryo have been ruled out by preimplantation diagnosis, one of them is inserted into the uterus until the woman becomes pregnant. Such a development will undoubtedly be enhanced if donor ova extracted from ovarian tissue obtained from aborted fetuses, become available. In animal experiments such ova have been successfully used for In Vitro Fertilization. Ovaries of 12 week

fetuses contain about 50 - 100 times more ova's than ovaries of 20 - 30 year old woman. Moreover, from a biological point of view they probably are of superior quality because they are younger than young. If such ova could also be deep frozen, this would open the avenue of creating large ova banks with eggs of superior quality. If, in addition it would become possible to characterize both male and female gametes, in the long run a couple might prefer the safe option of highly fertile gametes, with superior qualities and no genetic defects, instead of their own gametes. Complete DNA-characterization is expected to be a reality around the year 2000. It will be the fruits of the so-called Human Genome Project which is an enormous and coordinated endeavour of many prestigious scientific institutes all over the world. It will be a victory of progress in molecular biology and information technology. Becoming pregnant by using embryo's obtained from donor sperm and donor oocytes signifies the ultimate stage of the ongoing process of separating the biological linkage between sexuality and reproduction which started with the introduction of birth control methods. Such a development is likely to have a profound impact on male-female relations. If indeed parenthood is consciously postponed for two or more decades, relations until then are expected to be more transient and superficial. The pressure to find the Simon Pure within the short period before the approaching deadline of infertility will become less. Many partners, may be various at the same time become, an accepted feature of life, specially if AIDS becomes treatable and contraceptive barrier-methods are less cumbersome and clumsy.

Obviously all these changes will not happen from one day to the next, but because such developments are proceeding in small steps and are thus barely noticeable, there is a chance that they will be welcomed as the solution to many problems by many people, such as fathers and mothers and may be also by you.

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