

## CHAPTER 10

### *Infertility*

It sometimes seems that the world's women are divided between those desperately trying to avoid having children and those desperately trying to have them. One solution to this is, of course, adoption but, with abortion becoming more or less legal and more readily available and safer in many countries and contraception being very widely practised, the demand of children for adoption far outstrips supply in many countries.

Infertility has become almost as big a deal medically as unwanted fertility. Probably this has much to do with the realisation that the male is responsible for a couple's inability to have children about as often as is the female, coupled with the fact that there is no known cause in somewhere from 25 to 40 percent of these cases.

Furthermore, sperm counts have declined by about two percent a year for the past twenty years. The current favourite culprit is chemicals ubiquitous in the environment that masquerade as sex hormones. How much, if any, of male infertility is due to these chemicals is something that cannot yet be decided.

It would certainly not be the first time that toxins have been involved in infertility. In preindustrial Europe north of the Alps and Pyrenees, where rye bread was the staple food of the poor, fertility was suppressed by ergot alkaloids produced by a fungus on the rye. Lead was probably associated with decreased fertility in later Roman society (and lead levels have been steadily rising in countries with large numbers of motor vehicles burning leaded fuel).

Diet can also strongly affect fertility. Mary Matossian has put a good case that the fertility decline in Europe during the period 1875-1913 was due to new wheat milling methods and an increase in reliance on potatoes, which together resulted in a deficiency of zinc - an element required for fertility in both men and women. It might be worth looking at the zinc levels in the diet of modern men and women, especially vegetarians.

The decline of fertility in ancient Rome may well also have had something to do with the fact that they had hot baths up to three times a day. An hour's such exposure in males has been found to cause a decline in sperm production and motility lasting up to six weeks. That's why a man's testicles are suspended at a distance from the body. Even keeping them tight up against the body with 'jockey' briefs can probably contribute to lower sperm counts. Worst of all is strenuous bicycle riding in tight lycra pants. In fact, even men who spent long periods of the day sitting tend toward lower sperm counts. Even the higher temperatures experienced in summer can do it. So, what about refrigerated jocks? The idea has been mooted but so far noone has succeeded in making an appliance suitable for marketing.

Infertility in women is most commonly due to ovulatory failure or defect, tubal obstructions or adhesions, endometriosis, or uterine myomas. All these factors tend to rise with age, so that while one in seven couples in industrialised nations is infertile in the 30-34 age group, one in five of 35-39 year olds are. The fact that many women are delaying starting a family till later and later ages is definitely a factor in declining fertility.

Other lifestyle factors have been implicated, including consumption of caffeine (coffee, colas, tea, etc), marijuana, cocaine and other 'recreational' drugs. Anabolic steroids used in bodybuilding can cause complete sterility. Using artificial lubricants or douching can also damage sperm and prevent pregnancy. Again, if a woman has been using The Pill for years before she decides to start a family, it can take over a year after ceasing The Pill for her hormones to reestablish the normal pattern necessary for pregnancy.

If you are trying without success to have a baby, the first thing is to eliminate the harmful lifestyle factors above. Then, give yourselves the maximum chance by having intercourse in a man-on-top position every two days around the midpoint of the woman's menstrual cycle and abstaining from any form of sex that includes ejaculation (but not other forms; fondling and other sensual delights can help stop killing your whole sex life and can, in fact, help your prospects of

conceiving) for the other two days of this period. If this doesn't work in a year or so, you should seek medical help.

As stated above, there is about an equal chance of the male being at fault as of the female but, since female causes are usually easier to diagnose and can usually be treated more definitively, it is usual to start with the woman. If she is excessively thin and/or does not have periods, it is wise to investigate this first as a possible cause. Excessive weight loss, especially in anorexia nervosa and in women who train excessively (particularly runners, gymnasts, ballet dancers, cyclists) can lose so much body fat that they deplete their oestrogen (which is stored in subcutaneous fat) to levels insufficient for ovulation. The treatment is 'simply' for the woman to drastically reduce her training levels and to eat sufficient to restore her stores of body fat.

Detecting a woman's ability to ovulate used to be a fairly complex, laborious and inaccurate process of recording her temperature each morning immediately on awakening and before getting out of bed, to detect the tiny rise that occurs just after ovulation, due to the increase in progesterone production by the ovary. Today, it can be more easily and accurately achieved by measuring levels of luteinising hormone in the urine, to detect the surge that occurs 12-24 hours before ovulation.

There are many causes of failure to ovulate. One of the commonest, causing about a fifth of all infertility in women, is excessive production of the hormone, prolactin, by the pituitary. This can be detected by a blood test. Polycystic ovaries (affecting 3-5 percent of women of reproductive age), ovarian tumours, ovarian infections, autoimmune disease, ovarian damage resulting from irradiation or chemotherapy, genetic conditions affecting the ovaries, and severe disorders of the thyroid or adrenal glands can all cause lack of ovulation. If the specific cause can be identified and treated, fertility can often be restored as long as the ovaries are not permanently damaged.

If the ovaries are functional and treatment of any specific cause does not produce ovulation or if no specific cause can be found, it is often possible to induce ovulation by hormone treatment. The first treatment that is used is clomiphene, an oral medication that causes the pituitary to secrete luteinising hormone and follicle stimulating hormone, which act on the ovaries to cause ovulation. This works in about half of women treated. There is a six to seven times increase in the chance of a multiple birth.

If this does not work, a series of injections of human menopausal gonadotrophins may be given. These hormones act directly on the ovaries and produce ovulation in more than ninety percent of cases, with 60-70 percent becoming pregnant (15 percent with twins and five percent with triplets or more).

Blocked Fallopian tubes are usually caused by scarring after infection with a sexually transmitted disease (the cause of infertility in some two million women in the US alone). Blockage can probably best be detected by an X-ray method using a dye to outline structures in the uterus and tubes. Microsurgery is only successful in removing blockages in about 30-50 percent of cases.

Another major cause of female infertility is endometriosis, the growth of tissue lining the uterine cavity in places outside the uterus, which is the culprit in about fifteen percent of such cases. It is diagnosed by inserting a thin, lighted tube through a small incision in the abdomen and is treated either by surgery, which enables pregnancy in 40-65 percent of cases, or by drugs, such as danazol or nafarelin, which cause decreased oestrogen production and enable pregnancy in 40-50 percent of cases after 4-6 months treatment.

Rarer causes of female infertility include birth defects of parts of the reproductive system, other infections of the genital system, abnormal cervical mucus that impedes the passage of sperm, and antibodies to sperm. The immune reaction to sperm differs from allergy to semen in two important ways - the woman only reacts to sperm from some men; and she produces antibodies which destroy the sperm rather than harming herself. A woman's immune system can also sometimes attack parts of her own system that go toward making a baby.

Diagnosis and treatment of male infertility is rather more dodgy. The first step is always a semen analysis to determine if there are sufficient sperm of sufficient quality present. If not, there is often not much to offer beyond the simple suggestions offered earlier. However, it is always worth testing for hormonal factors. Correcting excessive prolactin secretion by treatment with bromocryptine or by surgically removing a prolactin-secreting tumour will cause an increase in sperm count and semen quality within 3-6 months. Pituitary hormone replacement using human menopausal gonadotrophins causes a 95 percent fertility rate in men who have a deficiency of luteinising hormone or follicle stimulating hormone and no other defect.

A condition that apparently can be linked to infertility is varicose veins in the scrotum. Surgical repair of these improves semen quality in about sixty percent of cases and 30-40 percent will go on to impregnate their partners. Surgery can sometimes also correct obstruction of the ejaculatory ducts, which is the cause of infertility in about five percent of men whose semen does not contain sperm.

Many societies have had (and a few still have) a tradition of a brother or other close relative of an infertile male inseminating his wife for him. These days, the process is usually performed using the semen of an anonymous donor by artificially introducing it into the vagina of the would-be mother. The pregnancy rate using frozen semen (now required in most places because of concerns about HIV) from a sperm bank is about sixty percent. Where the husband has a subnormal, but not too low, sperm count (i.e., more than about ten million per millilitre), his sperm may be used in a similar procedure. In the rare cases where the character of the woman's cervical mucus is inhibitory to fertilisation, direct introduction into the uterus may be useful.

Where the problem lies with the woman, things are not so simple, but there is at least now some hope. In vitro fertilisation can overcome such barriers to pregnancy as blocked or absent Fallopian tubes, severe endometriosis and immunologic infertility - but, in most cases, only in women younger than 35 with normal menstrual cycles and husbands with normal sperm counts. Even then, the success rate per attempt is only about fourteen percent and less than half of couples manage to have a baby after five attempts (this drops rapidly with age, to about 29 percent for women 35-39 and only 14 percent for those in their forties). It is also expensive and quite tedious for the woman. Firstly, daily hormone injections are used to stimulate egg production (these can cause pain, discomfort, mood swings, bloating, weight gain). About seven days later, a shot of another hormone causes the eggs to be released. Using a laparoscope with a hollow needle inserted at the navel into the follicles, the eggs are retrieved and placed in a petri dish containing a tissue culture medium duplicating that of the womb. Some 5-6 hours later, sperm are added and fertilisation occurs. The fertilised eggs are allowed to mature for about 48 hours before being placed in the uterus.

In women with at least one normal Fallopian tube, gamete intrafallopian transfer may give a better success rate (23-30 percent per attempt) than in vitro fertilisation. Here, sperm and eggs are placed directly into the Fallopian tube, where fertilisation (if it occurs) takes place.

Zygote intrafallopian transfer, in which the wife's eggs are fertilised by her husband's sperm in vitro and the fertilised transferred to the Fallopian tube within 24 hours, is also sometimes used and gives slightly better results (about sixteen percent per attempt) than regular in vitro fertilisation.

For women who don't ovulate or don't have ovaries or have a genetic defect they don't want to pass on to their children, egg donation, in which eggs harvested from another woman are used in an in vitro fertilisation procedure, produces similar results to methods using the woman's own eggs.

In recent years, another method of dealing with infertility has achieved some prominence - surrogate motherhood, where a woman carries a baby to term for a couple. One form of this involves a fertile husband and an infertile wife. The surrogate mother is artificially inseminated with the husband's sperm, carries the baby to term and then hands it over to the couple for adoption. In the other, the woman is able to produce ova but cannot, for one or other reason, carry

a baby to term. In this case, the usual in vitro fertilisation procedure is performed except that the fertilised ova are implanted in the uterus of the surrogate mother, who then carries the baby to term.

The whole business of assisted reproductive technologies (i.e., in vitro fertilisation and its variations, sperm and ova donation) raises a raft of legal and ethical issues that are still being addressed worldwide. The New York State Task Force on Life and Law last year produced a set of recommendations that are more or less typical of current thinking:

- ? The State should not regulate clinical technical issues, such as the number of embryos implanted in a given patient.
- ? The State should enact legislation establishing 'minimum standards for obtaining informed consent to assisted reproductive technologies'.
- ? The State should prohibit retrieval of gametes (i.e., sperm or ova) from dead people or living people who cannot give informed consent.
- ? The State should criminalise embryo theft or improper disposal.
- ? The State should establish means for children produced through assisted reproductive technologies to gain access to non-identifying information about gamete donors.
- ? The State should formalise a way for gamete donors to relinquish responsibility for children derived from their gametes.
- ? The State should not provide coverage for assisted reproductive technologies through public medical insurance programmes.
- ? Physicians may 'ethically decline to provide assisted reproductive services because of concerns about the welfare of a child who might be born'.