

Causes of Infertility

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INTRODUCTION

Infertility is described as the lack of conception after one year of unprotected intercourse (Bayer *et al.*, 2002). However, the amount of time after which treatment to a couple is administered varies considerably. It might be greatly reduced in the case of an obvious infertility problem, such as blockage of the fallopian tubes. Considering that there is an approximate 15-20% chance per month of achieving pregnancy, and that about 73-80% of couples achieve pregnancy before six months of trying, it is justified that an infertility evaluation and treatment are initiated after six months rather than one year of trying.

Infertility *per se* is not very common, affecting about 5-8% of the population in developed countries. What is more common, however, is the loss of early pregnancies. Various studies were carried out on women who ever experienced an early abortion, and certain trends in the results of these studies persisted from month to month. It was in fact observed that in any one month under normal conditions:

- 15% of oocytes fail to undergo fertilisation
- 10-15% of oocytes become fertilised and cleave, but fail to implant
- Only 42% of implanted ova succeed in suppressing the following menstrual period
- A further 24% lose their foetus after week four of gestation (Bittles and Matson, 2000).

New reproductive technologies are providing approximately 80% of infertile couples who seek treatment with offspring which is genetically related to both parents, whereas another 10-15% is also provided with pregnancy, however using donated gametes (i.e. offspring would be related to only one of the parents) (Fischel *et al.*, 2000).

It is important to stress that infertility is not only a medical problem, but it also involves many psychological, legal, moral and social issues, and hence administering the proper treatment becomes even more difficult. This in turn explains why, in a survey performed in the United States in 1995, it was discovered that despite of the availability of treatment only 21% of infertile couples ever sought

medical treatment. It is hence not difficult to conclude that infertility has a devastating emotional and psychological impact on any couple concerned.

CAUSES OF INFERTILITY

The causes of infertility are various and in some instances, a combination of factors may exist. Identifying the cause of infertility is the main key which will then lead to the administration of the appropriate treatment. This in turn points out the necessity of an accurate infertility evaluation.

FEMALE INFERTILITY

In about 45% of infertile couples, the cause of infertility lies within the female. In 30% of cases, there is male factor infertility whereas the remaining 25% are unexplained (Alper, 2002).

Ovulatory problems: In most cases where the woman is responsible for the infertility, the problem is ovulatory. In some instances, the woman might not be ovulating at all and this is evident when her menstrual cycle is irregular (the regular menstrual cycle is 23-39 days in length). Anovulatory cycles occur when the preovulatory surge of LH is not of sufficient magnitude to cause ovulation. This results in the failure of the corpus luteum to develop and hence no progesterone secretion takes place in the second portion of the cycle. Also, the cycle is shortened by several days but a rhythm is still observed (Guyton and Hall, 2000).

Over 90% of ovulatory problems can be treated with hormones, most of which are the same as those used in IVF programs. For example, in women with an inadequate stimulation from the hypothalamus, Gonadotropin-releasing Hormone (GnRH) is administered. This hormone stimulates the pituitary gland to release LH and FSH, which are in turn necessary for ovulation.

Sometimes the pituitary gland fails to produce sufficient amounts of LH and FSH. In such cases, Human Menopausal Gonadotropin (HMG) is given to the patient, which contains a mixture of approximately equal amounts of these two hormones.

When LH levels are abnormally high, the normal LH to FSH ratio is disrupted. This problem is usually corrected by administering FSH to the patient (Leese, 1988).

Another ovulatory problem is the luteal phase deficiency. In such cases, the menstrual cycle would be normal; however, there would be insufficient progesterone secretion during the luteal phase of the cycle. As a result, the endometrium doesn't mature enough to support implantation of the embryo. In this case, fertilisation would take place but early miscarriage would also follow (Bayer *et al.*, 2002).

The female may also be infertile due to ovulatory dysfunction, meaning that the ovaries are poorly developed, genetically abnormal or completely inexistent. This would in turn lead to hypogonadism i.e., less than normal secretion of ovarian hormones (Guyton and Hall, 2000).

Cervical problems: The cervix is the passageway which allows the spermatozoa to reach the uterine cavity and fallopian tubes. The cervical mucus lining the cervical canal is of great importance because it influences the sperm's motility and hence the sperm's access to the uterus. The pre-ovulatory follicle secretes estradiol which increases the quantity, consistency and water content of the mucus produced by the endocervical glands. In fact, at around mid-cycle, the water content of the mucus reaches a maximum of 95-98% and because of this a thin watery secretion spills out of the vagina and can be observed in the days the precede ovulation. During these days, spermatozoa can easily penetrate the mucus and gain access to the uterine cavity. As a result, inadequate production of cervical mucus as well as poor sperm quality will prevent the penetration of the mucus by the spermatozoa and hence pregnancy cannot be achieved. A problem of this sort is not amongst the commonest; it occurs in less than 5% of infertile couples (Bayer *et al.*, 2002).

Fallopian tubes problems: One of the commonest causes of female infertility is disease or damage of the fallopian tubes. In most cases, one or both tubes may be blocked and as a result, there can be no passage of ova, spermatozoa or embryos between the ovary and the uterus. Also common are damage to the mucosal lining, partial blockage and adhesions. The latter are characterised by strands of tissue which grow from diseased areas and keep the tubes fixed and unable to move, to pick up an ovum, for example (Leese, 1988).

Fallopian tubes problems are more common in women who had had an ectopic pregnancy or a ruptured appendix (Penzias, 2002). The use of IUDs increases the risk of pelvic inflammatory disease and hence tubal damage.

Uterine problems: A history of repeated miscarriages should immediately make the clinician think of uterine dysfunction. This can be confirmed by performing a Hysterosalpingogram (HSG). Uterine fibroids are quite common occurring in 15-20% of women over 35 years of age (Bayer *et al.*, 2002). Fibroids located within the cavity i.e., submucosal fibroids, have the greatest effect on fertility, whereas subserosal (outside the cavity) and intramural (within uterine wall) fibroids have minimal effect on fertility.

Exposure to Diethylstilbestrol (DES) causes impingement of the lateral walls of the uterus. Prominent uterine horns are another characteristic, creating a bicornuate shape. Other conditions which interfere with pregnancy include congenital anomalies such as unicornuate uterus and uterine septum. The former is usually accompanied by renal abnormalities and it also increases the chance of experiencing premature labour.

Another uterine anomaly which may interfere with pregnancy is Asherman's syndrome. This condition is characterised by intrauterine adhesions and hence large filling defects would be visible on an HSG.

MALE INFERTILITY

In approximately 30% of infertile couples, the infertility cause is male factor. In most of these cases, the problem is oligospermia, i.e., the semen would contain few spermatozoa or the sperm is of poor quality or motility. Azoospermia i.e., no sperm production, is far less common (Leese, 1988). In those cases where azoospermia is accompanied by normal gonadotropins, an obstructed outflow tract or congenital absence of the vas deferens are likely to be the cause for the absence of sperm in the semen (Bayer *et al.*, 2002). Certain anabolic steroids and other oral hormonal agents can cause oligospermia and sometimes even azoospermia. Medications which can affect spermatogenesis include cimetidine, spironolactone, isoniazid, calcium channel blockers and chemotherapeutic drugs-all of which must be taken into consideration when performing an infertility evaluation.

Sometimes, a male may have a normal number of spermatozoa but is still infertile. In such cases, approximately half of the spermatozoa are found to have abnormal morphology, such as, sperm with two heads, sperm with abnormally shaped heads, or even sperm with

two tails. Furthermore, in some cases the sperm may appear morphologically normal but its motility is entirely or relatively impaired (Guyton and Hall, 2000).

Another possible cause for male infertility is the varicocele, which is a dilated scrotal vein present in 25% of infertile males (Bayer *et al.*, 2002). Although the exact link between varicoceles and male infertility is not known, the most acceptable theory is that the dilated testicular vein raises the temperature of the testes above the optimal temperature thereby affecting spermatogenesis. (The optimal temperature for spermatogenesis is 2-3°F lower than core body temperature).

Male infertility may also be due to genetic defects, such as Klinefelter's syndrome, which may be detected by an elevated FSH level. However, an abnormal FSH level in males may also be due to sertoli-only-cell syndrome, previous mumps orchitis or prior cancer treatment. In cases of Kallmann's syndrome and hypothalamic dysfunction, both characterised by decreased or undetectable levels of FSH and LH, the infertility may be treated with FSH and Human Chorionic Gonadotropin (hCG), or with GnRH. (Bittles and Matson, 2000).

It is important to stress that IVF is not the solution to all infertility problems. Depending on the nature of the cause of infertility, the appropriate treatment must then be given. Therefore, an accurate and complete infertility evaluation is absolutely necessary in order to have a better understanding of the problems that are preventing the couple concerned from conceiving.

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