History of human artificial insemination

Willem Ombelet[1], Johan Van Robays[2]

[1]*Genk Institute for Fertility Technology, Department of Obstetrics and Gynaecology.*
[2]*Department of Pathology, ZOL, Campus St Jan, Schiepse Bos 6, 3600 Genk, Belgium.*

To whom correspondence should be addressed. E-mail: willem.ombelet@telenet.be

Abstract

Artificial insemination with homologous (AIH) or donor semen (AID) is nowadays a very popular treatment option for many subfertile women worldwide. The rationale for the use of artificial insemination is to increase gamete density at the site of fertilisation. The main reason for the renewed interest in artificial insemination is undoubtly the refinement of techniques for the preparation of washed motile spermatozoa. The sequence of events leading to today's common use of artificial insemination traces back to scientific studies and experimentation many centuries ago. Modern techniques used in human artificial insemination programmes are mostly adapted from the work on cattle by dairy farmers wishing to improve milk production by using artificial insemination with sperm of selected bulls with well chosen genetic traits. The history of artificial insemination is reviewed with particular interest to the most important hurdles and milestones.

Key words: Artificial insemination, assisted reproduction, history, human, intrauterine insemination, semen.

Introduction

The rationale behind artificial insemination is increasing the gamete density at the site of fertilization. Since many centuries different pioneers contributed to the history of artificial insemination, not only in humans but even more pronounced in farm animals. The primary reason for using this technique in farm animals is to speed up the rate of genetic improvement by increasing the productivity of food producing animals. This is accomplished by improving the selection differential wherein one highly selected male is mated with thousands of females. The AID industry was born.

For humans the situation is different: artificial insemination was originally developed to help couples to conceive in case of severe male factor subfertility of a physical or pschycological nature. Nowadays the process of AI is more commonly used in woman (lesbians or single women) with no male partner, in these cases the sperm is provided by a sperm donor. When donor sperm is used, the woman is the gestational and genetic mother of the child produced and the sperm donor is the genetic or biological father of the child.

Despite the extensive literature on the subject of artificial insemination with husband's semen, controversy remains about the effectiveness of this very popular treatment procedure, particularly in relation to IVF and ICSI (Cohlen 2005; Ombelet, 2005; Bensdorp *et al.,* 2007; Eshre Capri Workshop Group, 2009). Nevertheless, artificial insemination with husband's semen remains a widely used treatment option for many couples with unexplained infertility, cervical factor subfertility, physiologic or psychological sexual dysfunction and mild to moderate male subfertility.

Milestones in the history of artificial insemination

Unofficial history claims that the first attempts to artificially inseminate a woman were done by **Henry IV** (1425–1474), **King of Castile**, nicknamed *the Impotent*. In 1455, he married Princess

Fig. 1. — Picture of Antoni Van Leeuwenhoek (1632-1723)

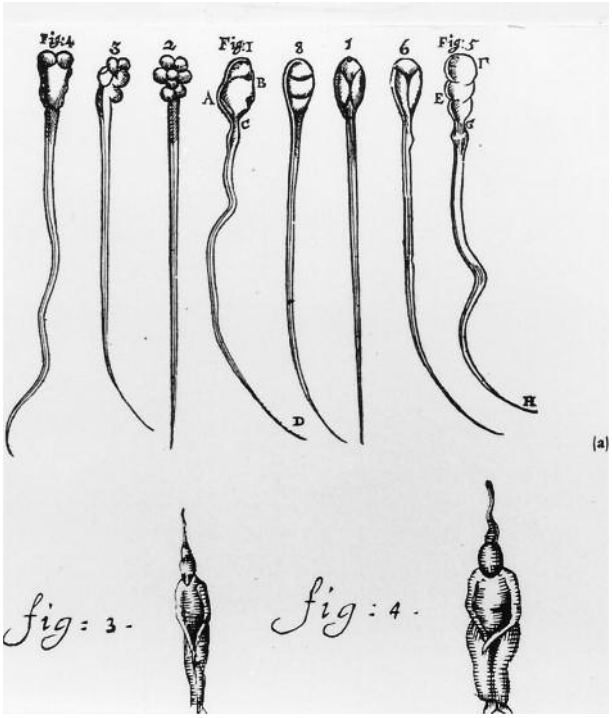

Fig. 2. — The 17th century conception of spermatozoa (A Van leeuwenhoek).

Juana, sister of Afonso V of Portugal. After six years of marriage she gave birth to a daughter, Joanna. Many contemporary historians and chroniclers assumed Henry was impotent. The possibility of artificial insemination was launched. Later on it was claimed that the princess was not the daughter of the king.

Fig. 3. — John Hunter (UK) wrote the first report of artificial insemination in medical literature in 1790.

Spermatozoa were first seen and described by **Antoni van Leeuwenhoek** and his assistant **Johannes Ham** in 1678. In a letter to William Bounker of the Royal Society the Royal Society of London (Phil.Trans. Vol. XII, nbr. 142, 1678) in which he showed a picture of sperm cells of the human and the dog. Van Leeuwenhoek described the spermatozoa as "zaaddiertjes" or "living animalcules in human semen ... less than a millionth the size of a coarse grain of sand and with thin, undulating transparent tails. He draws the conclusion that the tails must be operated by means of muscles, tendons and joints (Mol, 2006; Kremer, 1979). Van Leeuwenhoek did not study Latin, the scientific language of the day. Nevertheless, his paper amazed, and perhaps amused, the reigning King of England.

More than 100 years later, in 1784, the first artificial insemination in a dog was reported by the scientist **Lazzaro Spallanzani** (Italian physiologist, 1729-1799). This insemination resulted in the birth of three puppy's 62 days later (Belonoschkin, 1956; Zorgniotti, 1975).

The first documented application of AI in human was done in London in the 1770s by **John Hunter**, which has been called in medical history the "the founder of scientific surgery". A cloth merchant with severe hypospadias was advised to collect the semen (which escaped during coitus) in a warmed syringe and inject the sample into the vagina.

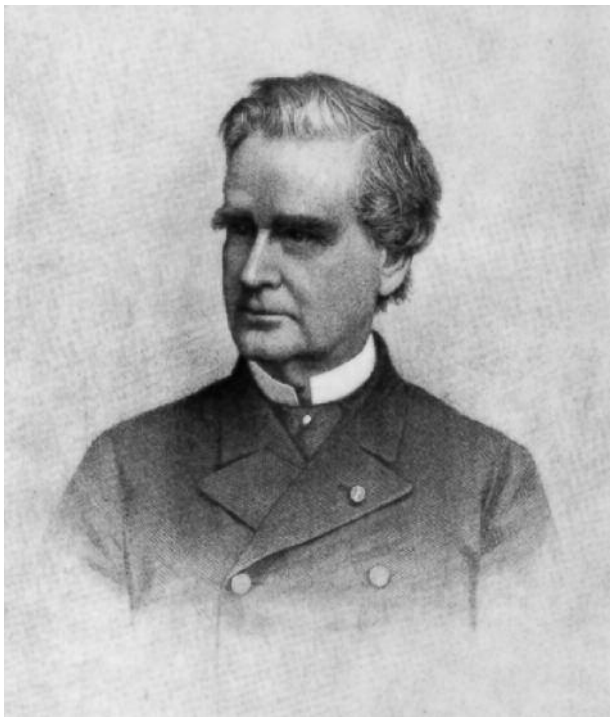

Fig. 4. — The first report of post-coital tests and the first description of 55 inseminations was done by JM Simms (US) in the 1850s (Source: South Med J, Lippincott, Williams & Wilkins 2004).

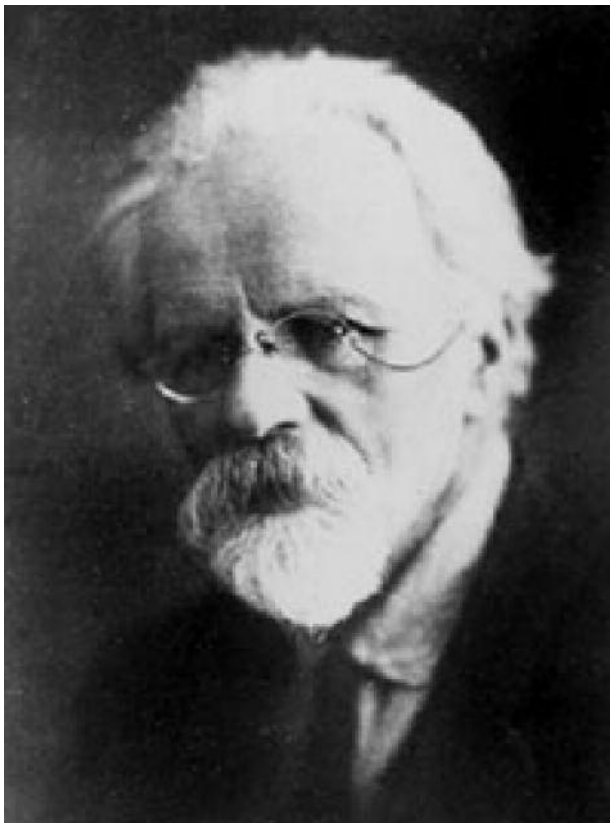

Fig. 5. — Ilya Ivanovich Ivanov (Russia) developed the methods of artificial insemination as we know them today in 1922.

J Marion Sims reported his findings of postcoital tests and 55 inseminations in the mid 1800s. Only one pregnancy occurred but this could be explained by the fact that he believed that ovulation occurred during menstruation. JM Simms was born in Lancaster County (USA) in 1813. In 1863 he began writing his innovative work *Clinical Notes on Uterine Surgery*, which was controversial but widely read. Its revolutionary approach to female diseases was refreshing, and its emphasis on treatment of sterility, including artificial insemination, was ahead of its time.

In 1899 the first attempts to develop practical methods for artificial insemination were described by **Ilya Ivanovich Ivanov** (Russia, 1870-1932). Although Ivanov studied artificial insemination in domestic farm animals, dogs, rabbits and poultry, he was the first to develop methods as we know today, also in human medicine. The work of Ivanov was taken over by **Milovanov**, another Russian scientist. He published his paper on "Artificial insemination in Russia" in the Journal of Heredity in 1938. The innovating work in Russia inspired **Eduard Sörensen** from Denmark to organize the first cooperative dairy AI organization in Denmark in 1933, followed by the introduction of the first AI co-operative in the US in 1938 by **EJ Perry**, a dairyman from New Jersey. In the US and other Western countries the number of AI cooperatives increased rapidly. Nowadays more than 90% of dairy cows are artificially inseminated in the Netherlands, Denmark and the United Kingdom.

Considering humans, only after the introduction and availability of donor sperm artificial insemination became very popular (AID). For many years homologous artificial inseminations were only indicated in cases of physiologic and psychologic dysfunction, such as retrograde ejaculation, vaginismus, hypospadias and impotence.

With the routine use of post-coital tests other indications were added such as hostile cervical mucus and immunologic causes with the presence of antispermatozoal antibodies in the cervical mucus.

The first reports on human artificial insemination originated from Guttmacher (1943), Stoughton (1948) and Kohlberg (1953a; 1953b). It was the real start of a new era in assisted reproduction.

Other important research discoveries in animal studies undoubtly influenced the development of artificial insemination, also in human. **Phillips and Lardy** (1939) were the first to use egg yolk to protect bull sperm cells from temperature shock upon cooling. This protection was explained by the effect of phospholipids and lipoproteins in the egg yolk. **Salisbury et al.** (1941) improved the media by using egg yolk with sodium citrate, permitting the

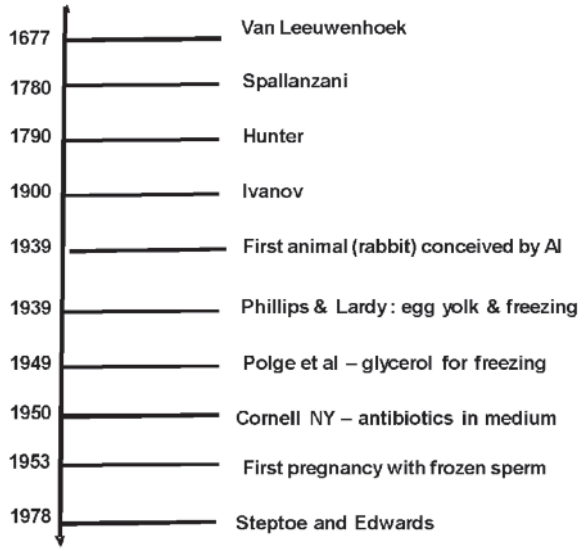

Fig. 6. — Most important milestones in the history of artificial insemination.

use of semen at 5° C for up to three days. **Polge and co-workers** (1949) were the first to freeze fowl and bull spermatozoa by using glycerol in the extender media. In 1950 Cornell University scientists (New York) discovered that antibiotics could be added to the sperm solution in artificial insemination processes. The so-called Cornell extender (**Foote and Bratton**, 1950) contained the antibiotic mixture of penicillin, streptomycin and polymyxim B and was used for many years as the standard. Antibiotics are presently still used for the protection against possible contamination.

In 1953 the first successful pregnancy from artificial insemination with frozen and thawed sperm was reported, a major breakthrough in history.

Considering all these new developments, it was not surprising that in the 1970s the sperm bank industry became very popular and commercialized, especially in the United States.

The IVF revolution

The main reason for the renewed interest in artificial insemination in human was undoubtly the introduction of in-vitro fertilisation (IVF) in 1978 by **Steptoe and Edwards**. Due to this new technique, methods for the preparation of washed motile spermatozoa were refined and examined. These washing procedures are necessary to remove prostaglandins, infectious agents and antigenic proteins. Another substantial advantage of these techniques is the removal of nonmotile spermatozoa, either leucocytes or immature germ cells. This may be an important factor in enhancing sperm quality by a decreased release of lymphokines and/or cytokines and a reduction in the formation of free oxygen radicals after sperm preparation. Most popular are the swim-up procedure, the discontinuous Percoll gradient method, the mini-Percoll (small volume) gradient technique and the use of Sephadex columns. The final result is a better sperm fertilising ability in vitro and in vivo (Aitken and Clarkson, 1987). As a consequence of these improved sperm selection techniques, the use of artificial insemination became very popular as a cost-effective first line treatment procedure in case of mild to moderate male factor infertility.

Legal, socio-cultural and religious considerations surrounding artificial insemination

The moral and social implications of artificial insemination were debated in both the medical and popular press in the United States since 1909, in Europe the debate started in the 1940s. The Catholic Church objected to all forms of artificial insemination, saying that it promoted the vice of onanism and ignored the religious importance of coitus. The main criticism was that AI with donor semen was a form of adultery ***promoting the vice of masturbation***. Other critics were concerned that AID could ***encourage eugenic government policies***.

Nevertheless, the demand for donor sperm increased tremendously. After the first successful pregnancy from frozen sperm, reported in 1953, the development of a thriving sperm-bank industry starting in the 1970s and the commercialization of AID became unavoidable. The growing number of AID‘s raised new concerns leading to new regulations. The following measurements became common practice: because of the possible transmission of sexually transmitted diseases, including HIV, by the use of fresh sperm screening for infections of donors and donations has become required by many local and national governments. The use of fresh semen samples almost disappeared. Another concern is the possibility to donate semen many times. In order to diminish the chances of unknowing marriage of biological siblings among AID children some government regulations tightly restrict the number of times a single donor’s semen may be used and/or restrict the number of children by a given donor.

Sociocultural concerns with biological paternity and the maintenance of the heterosexual, married couple as the basis of the family remains important in many countries. A lot of countries all over the world have not approved the use of AI with donor semen for single women and lesbian couples yet. Another point of debate is whether the donor has to be anonymous or non-anonymous, and when to

inform and what to tell AID children about their biological parentage, if non-anonymous donors are used. Is it possible and/or advisable to use sperm of relatives, such as brothers or the father? Whether or not to pay the donors is another point of discussion and recently more and more questions about sexing of sperm by DNA quantification using flow cytometry instrumentation.

Conclusion

Treatment with artificial insemination with husband's sperm seems to be a valuable first choice treatment before starting more invasive and more expensive techniques of assisted reproduction in many cases of human subfertility. It is a simple and non-invasive technique which can be performed without expensive infrastructure. laboratory infrastructure are mandatory. Many of the principle nowadays used in human artificial insemination are adapted from domestic animal studies, especially from cattle. The use of frozen/thawed donor samples and the renewed interest in sperm washing procedures due to the introduction of IVF were the most important milestones in the history of AI. The increasing demand of lesbians and single women for AI with donor semen is another challenge for the future in many countries worldwide. Many debates, socio-cultural and ethical, are to be expected in the near future, the use of sexing of sperm by DNA quantification will be one of them.

References

Aitken RJ, Clarkson JS. Cellular basis of defective sperm function and its association with the genesis of reactive oxygen species by human spermatozoa. J Reprod Fert. 1987;81:459-69.

Belonoschkin B. The science of reproduction and its traditions. Int J Fertil. 1956;1:215-24.

Bensdorp AJ, Cohlen BJ, Heineman MJ, Vandekerckhove P. Intra-uterine insemination for male subfertility. Cochrane Database Syst Rev. 2007;(4):CD000360.

Cohlen BJ. Should we continue performing intrauterine inseminations in the year 2004? Gynecol Obstet Invest. 2005;59:3-13. Review.

ESHRE Capri Workshop Group. Intrauterine insemination. Hum Reprod Update. 2009;15:265-77.

Foote RH, Bratton RW. The fertility of bovine semen in extenders containing sulfanilamide, penicillin, streptomycin, and polymyxin. J Dairy Sci. 1950;33:544-7.

Guttmacher AF. The Role of Artificial Insemination in the Treatment of Human Sterility.

Bull NY. Acad Med. 1943;19(8):573-91.

Ivanoff EI. On the use of artificial insemination for zootechnical purposes in Russia. J Agric Sci. 1922;12:244-56.

Kohlberg K. The practice of artificial insemination in human. Dtsch Med Wochenschr. 1953;78:835-9.

Kohlberg K. Artificial insemination and the physician. Dtsch Med Wochenschr. 1953;78:855-6.

Kremer J. The significance of Antoni van Leeuwenhoek for the early development of Andrology. Andrologia. 1979; 11:234-49.

Leeuwenhoek A. De natis è semine genital animalculis. R. Soc. (Lond.) Philos Trans. 1678;12:1040-3.

Milovanov VK. Artificial Insemination of Livestock in the U.S.S.R. Trans. By Birron A and Cole ZS. 1964; S Monson, Jerusalem Tech. Services, US Dept Commerce, Washington, DC.

Moll WAW. Antonie van Leeuwenhoek. http://www.euronet.nl/users/warnar/leeuwenhoek.html. © 2006

Ombelet W. IUI and evidence-based medicine: an urgent need for translation into our clinical practice. Gynecol Obstet Invest. 2005;59:1-2.

Perry EJ. The Artificial Insemination of Farm Animals. 4th ed. Rutgers University Press, 1968. New Brunswick, New York.

Phillips EJ, Lardy HA. A yolk-buffer pabulum for the preservation of bull semen. J Dairy Sci. 1940;23:399-404.

Polge C, Smith AU, Parkes AS. Revival of spermatozoa after vitrification and dehydration at low temperatures. Nature. 1949;164-6.

Salisbury GW, Fuller HK, Willett EL. Preservation of bovine spermatozoa in yolk-citrate diluents and field results from its use. J Dairy Sci. 1941;24:905-10.

Sörensen E. Insemination with gelatinized semen in paraffined cellophene tubes. Medlernsbl Danske Dyrlaegeforen. 1940;23:166-9.

Spallanzani L. Dissertations relative to the natural history of animals and vegetables. Trans. By T. Beddoes. J. Murray, London. 1784; Vol 2:195-9.

Steptoe PC, Edwards RG. Birth after reimplantation of a human embryo. Lancet. 1978;12;2(8085):366.

Stoughton RH. Artificial human insemination. Nature. 1948; 13;162(4124):790.

Zorgniotti AW. The spermatoa count – a short history. Urology. 1975; 5:672-3.