16 Optimizing Technique in Follicular Aspiration and Flushing

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SUMMARY

Optimizing the number of oocytes retrieved during oocyte retrieval in minimal stimulation *in vitro* fertilization (IVF) is one of the most challenging steps, with every additional egg influencing the pregnancy rate.

Interestingly, a series of publications during the late 80s and early 90s, comparing the effect of single lumen needles with double lumen needles with flushing and non-flushing follicles concluded that the numbers of oocytes in both arms of studies were comparable, however, the retrieval time and pain for patients in whom the double lumen needle was used was increased. Unfortunately, the authors of these studies ignored the law of Physics, in particular, Poiseuille's law, characterizing the flow dynamics of fluid through pipes. Nowadays, about 50% of the egg retrievals worldwide are performed with single lumen needles and non-flushing as consequence of those studies. In my view, a few, approximately 15-20% of oocytes were missed and some thousands of children would have been born using consequent flushing during ovum pick-up (OPU) in IVF in the past three decades.

The introduction of mild IVF, semi-natural IVF and natural cycle IVF must be the reason for the renaissance of the flushing techniques. The current techniques of oocyte retrieval *in vitro* maturation (IVM), inserting the needle into ovary, withdrawing the needle up to more than 10 times in order to flush it outside patient's body, was, for me, the trigger to invent a totally new needle and flushing system, which enables physicians to flush even very small follicles as small as 3 mm in diameter. The details will be presented in this chapter.

INTRODUCTION

History

The first approach to the ovaries in ovum pick-up (OPU) in IVF was transabdominal by laparoscopy.[1] This was followed by transabdominal ultrasound-guided oocyte retrieval[2] and then by transvaginal aspiration under transabdominal ultrasound guidance.[3]

The first OPU with vaginal ultrasound was published in 1985 by Wikland and Hamberger[4] and remains the standard of care.

Brinsden in 1992 said "We believe that the use of vaginal ultrasound has enabled the technique of oocyte recovery to be refined down to the least invasive, least painful, most accurate and most simple method that we are likely to be able to achieve in the foreseeable future".[5]

Manual aspiration with syringes has been supplanted by electronic aspiration pumps, which can maintain a steady aspiration pressure of about 120 mm Hg. Flushing follicles, with the use of double lumen needles or single lumen needles with 3-way valves, has widely been used in order to optimize oocyte retrieval rates.

In the late 80s and early 90s', a series of papers were published comparing OPU with single lumen needles without flushing vs. double lumen needles with flushing, ignoring the laws of physics. Most authors compared the two needles with same outer diameter, not considering the dramatically narrowed inner diameter of inner needle in double lumen needles.[6-11] In each of 1139 treatment cycles, Knight et al.[10] found no statistical differences either in the total number of oocytes collected or in the pregnancy rates, but an increase in the operation time and anesthetic requirements in the flushing group. They concluded that flushing was "superfluous".

In contrast, Baghtaria and Haloob,[12] compared oocyte retrieval rate with one 16-gauge double-lumen needle without flushing and with flushing four times at 170 mm Hg.

About 40% of oocytes were retrieved with aspiration only, 82% of oocytes were retrieved with two flushes, and 97% with four flushes. Only 3% of remaining oocytes were retrieved with the 5th and 6th flush. Flushing up to four times would not make a difference in operating and anesthetic time, with minimum cost implications. However, it would allow a maximum number of oocytes (up to 85%) to be retrieved with four flushes, especially in patients with few follicles. Lozano et al.[13] found a doubling in the pregnancy rate following flushing in semi-natural cycles IVF. The oocytes obtained by follicular flushing had the same reproductive potential compared those obtained in follicular fluid.

Simple Basics of Physics for Aspiration and Flushing of Fluids in Pipes

Reeves got to the point, when he wrote 1989: "The laws of physics, applicable to a device, such as an ovum pick-up

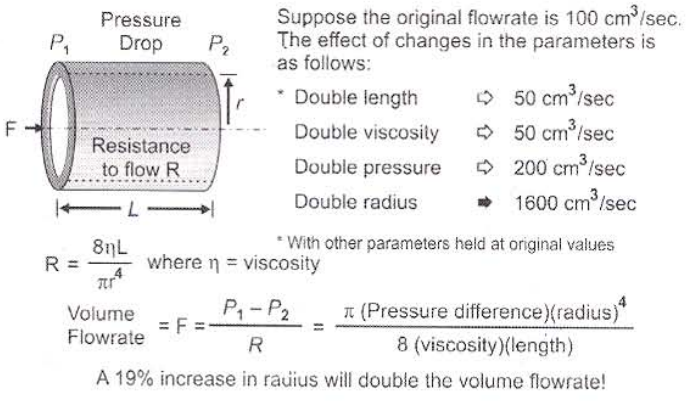

Fig. 16.1: Poiseuille's law

needle, are those relating to the flow of fluid through pipes, in particular, Poiseuille's law" (Fig. 16.1). This law takes into consideration the lumen diameter and the length of the conduit; in this case, the length of the needle and the tube carrying the egg to the collecting container. The other parameters are the viscosity of the fluid and the force applied, in this case, vacuum.

Obviously, the success of the exercise is judged by the number of eggs collected in relation to the number of follicles available; however, the law of physics used to collect the eggs are either frequently ignored or not considered.[14]

Example 1: Figure 16.2 compares two needles with the same outer diameter same length, same aspiration pressure, and same tubing. Aspiration of 8 mL of fluid takes a third of the time with single-lumen needle in comparison with a double-lumen needle. This is because the inner diameter of the single-lumen is 1.2 mm compared with 0.9 mm for the double-lumen needle.

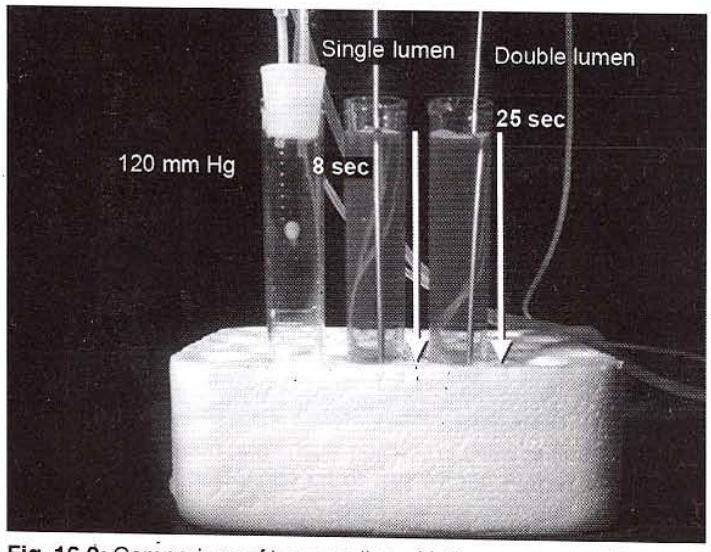

Fig. 16.2: Comparison of two needles with the same outer diameter, same length, same aspiration pressure, and same tubing. Comparison: Single lumen needle (1.5-gauge) takes 3 times shorter aspiration time than double lumen needle (1.5-gauge) *(For color version see Plate 6)*

Example 2: Comparison of the aspiration time of 8 ml of fluid. Same 18-gauge needle of 35 cm length and 90 cm length of tubing.

A. Inner diameter of tubing: 1.2 mm; aspiration time: 15 sec
B. Inner diameter of tubing: 0.9 mm; aspiration time: 32 sec

CLINICAL DISCUSSION

Innovative Devices for Oocyte Retrieval and Follicular Flushing

Invented, Patented and Prototyped by Dr Hans-Peter Steiner: At the end of 2007, I attended an *in vitro* maturation (IVM) workshop in Vienna, Austria, held by Ri-Chen Chian, McGill University, Montreal. I was told that the common practice for oocyte retrieval in IVM is to use a 19-gauge single lumen needle. After aspiration of several follicles, the needle is withdrawn, flushed with heparinized saline and reinserted again. I saw an egg retrieval procedure in IVM in which the needle was reinserted 13 times. This technique requires a remarkably longer time compared with classical IVF because of repeated flushing of the needle and the tubing in order to prevent the blockage, and is painful for the patient. General anesthesia is more frequently needed than for conventional IVF.

After this workshop, I began to speculate how to make oocyte collection in IVM more comfortable for the patient and for the physician. I invented a new technique to flush a single-lumen needle from outside the needle without narrowing the inner lumen.

Steiner needle (Fig. 16.3): This is a quasi double lumen needle with the double lumen starting 7 cm proximal of the needle tip, preferably 18-gauge, down to even 22-gauge, for IVM and a 17-gauge needle for conventional IVF. After drilling 2 small holes into the needle, located about 7 cm proximal of the needle tip, communication with a plastic tubing makes it possible to flush the needle from outside. The final version of the Steiner needle set will have a disposable needle guide to be clicked at a metallic, autoclavable half pipe, which can be fixed to an ultrasound probe covered by condom or cover in order to achieve a totally disposable product according modern hygienic standards. Figure 16.4 illustrates the comparison between the double lumen needle and the Steiner needle.

Due to special fluid dynamics of the Steiner needle, it is possible to flush small follicles in IVM with 18- or 19-gauge single lumen needles up to 4 times within a few seconds in a pulsative manner under continuing aspiration pressure and overpowering aspiration pressure by the Steiner flush. The Steiner flush (Fig. 16.5) is a totally mechanical flushing pump, activated by the physician's foot via a cable. The optimal aspiration pressure is 120 mm Hg. Withdrawing the needle from the ovary is necessary only when one has to change from one ovary to the other. This procedure minimizes the time of

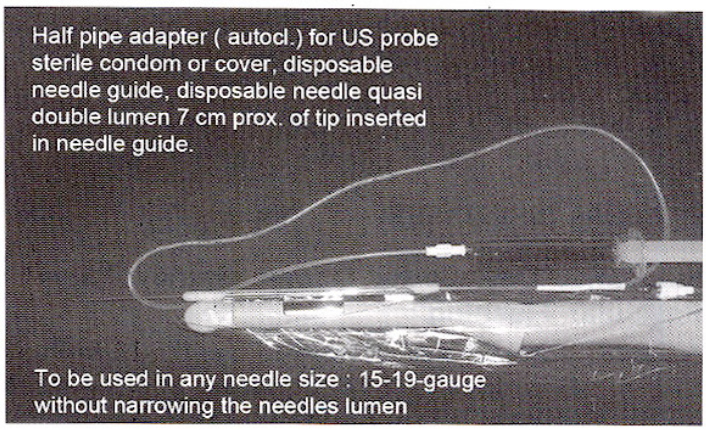

Fig. 16.3A: The Steiner needle: Steiner needle for mild IVF, IVM and normal IVF *(For color version see Plate 6)*

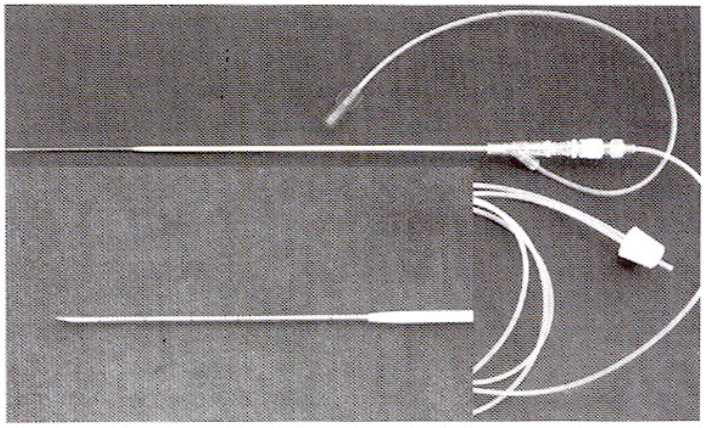

Fig. 16.3B: The Steiner needle with the quasi double lumen, 7 cm proximal of needle tip *(For color version see Plate 6)*

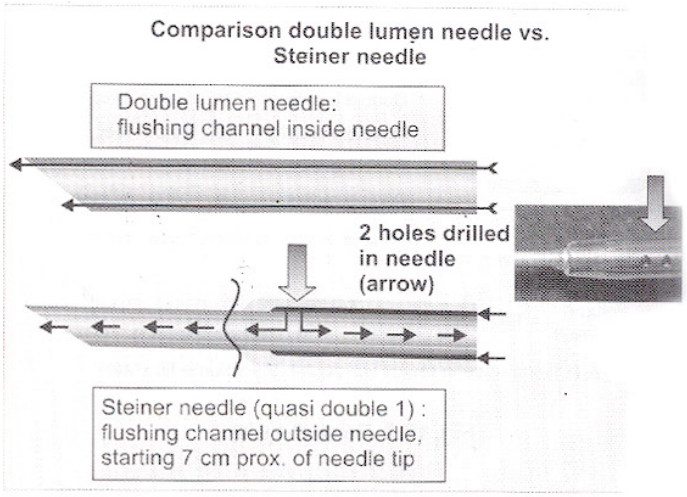

Fig. 16.4: Comparison of the double lumen needle vs. the Steiner needle

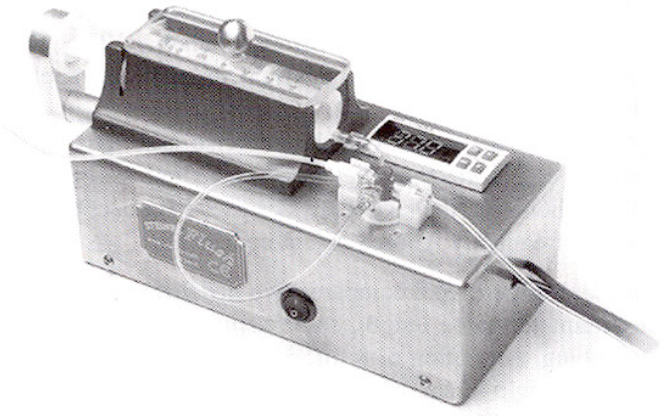

Fig. 16.5: The Steiner Flush with syringe warmer *(For color version see Plate 7)*

oocyte collection, optimizes the number of retrieved oocytes, and minimizes contamination of the oocyte-cumulus complex (OCC) with blood.

Video and computer animation of the egg retrieval procedure with the technique can be watched at www.ivfetflex.com.

Steiner valve in combination with Steiner flush

The Steiner valve, with electric motor, is integrated in flushing pump. A3-way valve can be clicked at the Steiner valve (Figs 16.6 and 16.7).

Option I: Steiner needle for small IVM follicles: electric button switched off. 3-day valve remains in position aspiration.

Option II: Steiner needle for normal IVF: electric button switched on.

As soon as the physician activates the pedal of the Steiner flush, an electric motor in the Steiner valve turns the 3-way valve from the 'aspiration' to the 'flush' position. The operator can adjust the individual pressure and amount of fluid during flushing. Moving the pedal back to the starting position reopens the aspiration line. The advantage is that repeated and stressful manual manipulation of the stop cock is no longer necessary during flushing. A syringe warmer guarantees constant temperature at 37°C.

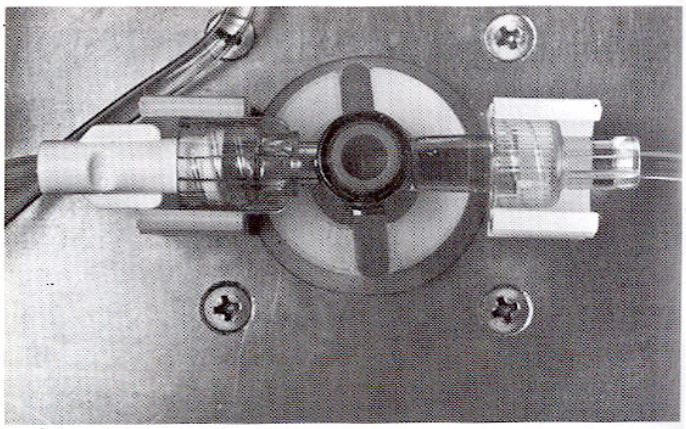

Fig. 16.6: Steiner valve in position 'flushing' in normal IVF. Flushing tube of the Steiner needle has to be connected with the syringe directly *(For color version see Plate 7)*

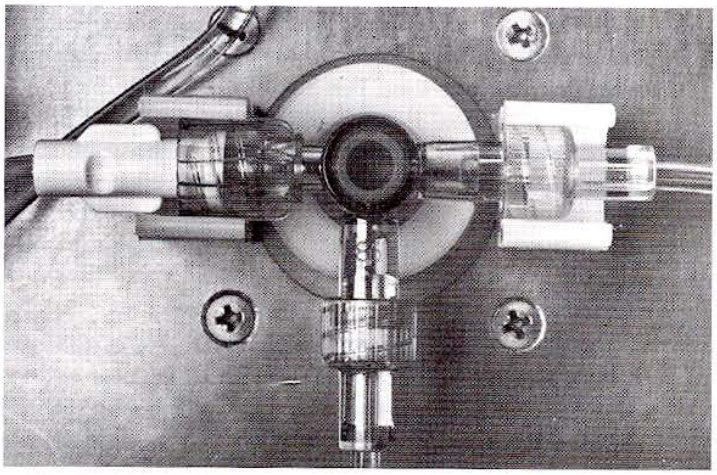

Fig. 16.7: Steiner valve in position 'aspiration' in combination with a conventional single lumen needle can be used with any single lumen needle with a luer *(For color version see Plate 7)*

Option III: With conventional single lumen needle with a luer in normal IVF.

Gauge Finding Study

The aim of this study was to find the optimal needle size for oocyte retrieval needles for normal IVF. In a pilot study, we used an 18-gauge Steiner needle with an outer diameter of 1.2 mm, inner diameter of 0.8 mm, and a 90 cm tubing with an inner diameter of 1.5 mm. Due to a dead space in the Steiner needle of only 7 cm, which enables flushing of the remaining needle plus tubing, it was possible to compare the effect of flushing and non-flushing with same needle. The small dead space can be ignored. In 31 patients, 543 follicles (averaging 17.5 follicles per patient) were punctured and 339 oocytes were aspirated. Table 16.1 shows the number of oocytes aspirated.

The results are displayed in Figure 16.8. The percentages in the Figure 16.8 refer to the number of oocytes collected from the 543 follicles, whereas the percentages in Table 16.1 describe the proportion of the oocytes.

The results indicate that moderate flushing approximately doubles the number of collected oocytes, whereas extensive flushing only marginally increases the number of oocytes. Our results show that flushing with appropriate instrumentation can significantly increase the number of retrieved oocytes.

We believe that a 17-gauge Steiner needle could result in increased oocyte retrieval compared to 18-gauge needles and combine the effect of increased turbulences, resulting in minimized aspiration time and sufficient number of oocytes. Using a double lumen needle at a same inner diameter as the Steiner needle for flushing, Baghtaria and Haloob[12] reported results similar to that observed in our study: 40% of the oocytes collected without flushing and 42.5% collected with 1 or 2 flushes (compared with 45% and 47% respectively in our series).

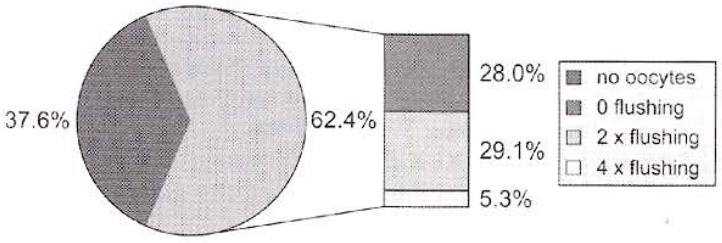

Fig. 16.8: Gauge finding study *(For color version see Plate 7)*

Table 16.1: Gauge finding study. Relation between flushing and the number of oocytes aspirated

Characteristics	*Number*	*Percent*	*Cumulative percentage*
No oocytes aspirated	204/543	(37.6%)	
Oocytes aspirated	339/536	(62.4%)	
without flushing	152/339	(44.8%)	(44.6%)
2 x flushing	158/339	(46.6%)	(91.4%)
4 x flushing	29/339	(8.6%)	(100.0%)

Though results of a satisfactory oocyte retrieval rate associated with flushing the follicles twice, not observed without flushing, seem encouraging, a randomized study is needed to support the hypothesis that the 17-gauge Steiner needle combines the effect of increased turbulences by shortening aspiration time, together with the option of flushing to collect an optimal number of oocytes.

CONCLUSION

Since we began IVF in 1988, I have flushed follicles at least once during oocyte retrieval under mild sedation and analgesia. In cases involving poor responders, where mild or natural cycle IVF is applicable I flush follicles 4 times or more. From a technical point of view, in my experience, the aspiration time for each 20 mm follicle should be, at the most, 8-10 seconds. This creates sufficient turbulences in follicles and optimizes the release of oocyte-cumulus complexes (OCC). It is advisable to adjust the aspiration pressure to achieve this functional characteristic.

Manufacturers of ovum pick-up sets for conventional IVF must consider an inner lumen of aspiration needles of at least 1.0 mm and an inner lumen of tubing of at least 1.2-1.3 mm to achieve a limited aspiration time and optimal turbulences for each follicle. IVM needles are generally smaller, with an inner diameter of 0.8 mm. Even with IVM needles, the Steiner needle technique permits needle flushing and optimizes oocyte retrieval rates. Aspiration time and patient discomfort are reduced and pregnancy rates are hopefully increased. I hope to change the paradigm of non-flushing follicles towards flushing with my inventions.

REFERENCES

1. Steptoe PC, Edwards RG. Laparoscopic recovery of preovulatory human oocytes after priming of ovaries with gonadotropins. Lancet 1970;1:683-689.
2. Lenz S, Lauritsen JG, Kjellow M. Collection of human oocytes for in vitro fertilization by ultrasonically guided follicular puncture. Lancet 1981;317:1163-1164.
3. Gleicher N, Friberg J, Fullan N, Giglia RV, Mayden K, Kesky T, Siegel I. Egg retrieval for in vitro fertilisation by sonographically controlled vaginal culdocentesis. Lancet 1983; 322:508-509.
4. Wikland M, Enk L, Hamberger L. Transvesical and transvaginal approaches for the aspiration of follicles by use of ultrasound. Ann NY Acad Sci 1985;442:182-194.
5. Brinsden PR, Rainsbury PA. Editors, In Vitro Fertilization and Assisted Reproduction. The Parthenon Publishing Group, 1992.
6. Scott RT, Hofmann GE, Muasher SJ, Acosta AA, Kreiner DK, Rosenwaks Z. A prospective randomised comparison of single- and double-lumen needles for transvaginal follicular aspiration. J In Vitro Fert Embryo Transfer 1989;6:98-100.
7. Kingsland C, Taylor CT, Aziz N, Bickerton N. Is follicular flushing necessary for oocyte retrieval? A randomized trial. Hum Reprod 1991;6:382-383.
8. Waterstone J, Parsons JH. A prospective study to investigate the value of flushing follicles during transvaginal ultrasound directed follicle aspiration. Fert Steril 1992;57:221-223.
9. Tan SL, Waterston J, Wren M, Parsons J. A prospective randomized study comparing aspiration only with aspiration and flushing for transvaginal-directed oocyte recovery. Fertil Steril 1992;58:356-360.
10. Knight DC, Tyler JP, Driscoll GL. Follicular flushing at oocyte retrieval: A reappraisal. Aust N Z J Obstet Gynaecol 2001; 41:210-213.
11. Levens ED, Whitcomb B, Payson M, Larsen F. Ovarian follicular flushing among low-responding patients undergoing assisted reproductive technology. Fertil Steril 2008;91:4:1381-1384.
12. Bagtharia S, Haloob AR. Is there a benefit from routine follicular flushing for oocyte retrieval? J Obstet Gynaecol 2005;25:374-376.
13. Méndez Lozano DH, Fanchin R, Chevalier N, Feyereisen E, Hesters L, Frydman N, Frydman R. The follicular flushing duplicate the pregnancy rate on semi-natural cycle IVF. J Gynecol Obstet Biol Reprod (Paris) 2007;36:36-41.
14. Reeves G. Letter to the editor. J In Vitro Fert Embryo Transfer 1989; Vol.6, No.6: 353-354.

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