# NaProTechnology (NPT) – After previously unsuccessful Artificial Reproductive Technology (ART)

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## INTRODUCTION

Infertility is a significant problem for many couples in the developed world today. Up to 1 in 5 couples experience difficulty conceiving in the United States[1]. In Europe 1 in 6 couples have difficulty conceiving[2]. Current infertility protocols usually advise **blood tests on day 3 to 7** of the menstrual cycle to assess gonadotrophin and prolactin levels, thyroid function, hemoglobin, rubella status and testosterone levels – if clinically indicated. In addition bloods tests are usually taken on **day 21 or 22** of the cycle to measure progesterone levels in the probable mid-luteal phase of the menstrual cycle. **Most specialists would agree that ovulation is probably occurring if progesterone levels exceed 30 nmol/l (9.5 ng/dl).** After a seminal fluid analysis, post-coital test, ultrasound examination, laparoscopy and dye test and possibly a six to nine month trial of clomid those couples who have not conceived face the prospect of Artificial Reproductive Technology (ART) if they wish to continue fertility treatment. Occasionally ovulation induction with FSH (with or without intrauterine insemination) may be given for a further 3 to 6 cycles before embarking upon In Vitro Fertilization (IVF) or Intra-cytoplasmic Sperm Injection (ICSI), which we refer to as ART throughout this chapter.

NaProTechnology (NPT) is a new, safe and effective means of treating infertility that can avoid the perceived need for ART in many cases. NaProTechnology is a couple-centered, disease-based approach to investigate, diagnose and treat infertility. The term "Natural" refers to the method of conception through a natural act of intercourse as opposed to any artificial intervention which replaces intercourse. Clinical experience and retrospective studies[3] show great promise, however further prospective studies are needed to determine present day success rates and convince the greater medical community of the value of NPT fertility treatment.

Ideally couples should learn how to track the signs of fertility and understand their fertility potential, even before attempting conception. Couples who use Creighton Model Fertility*Care*™ System[4] (CrMFCS) for family planning have a distinct advantage over non-users. They can tell, even before they try to conceive, if they may be at risk of miscarriage or infertility based on their CrMFCS charting pattern. This is very useful information to help them make an informed decision about managing their fertility in a way which is appropriate to them. If couples experience infertility or miscarriage NPT should be their first choice to identify and treat whatever abnormalities may be found.
But what about couples who were unaware of the NPT approach and have tried all of the medical treatments available to them, including artificial reproductive technologies (ART) without success? Is it worth trying NPT at this point or are they simply wasting their time?

Experience from a Family Practice in Galway, Ireland has shown that 20% to 30% of couples with previously unsuccessful ART will have a successful pregnancy with NPT. This chapter will look at that select group of patients who have succeeded with NPT after failed ART.

## BACKGROUND

NPT has been available to Irish patients since 2nd Feb 1998. It was not known at that time how effective this treatment would be for infertile couples who had otherwise finished with fertility treatment. Patients were told that because NPT was a new approach we could not predict what the probability of success would be.

This Chapter will focus on the number of couples who have conceived with NPT, despite previously failed ART. We will look at 6 years of clinical practice in a Family Physician's office from the beginning of Feb. 1998 until Feb. 2004. The percentage success rate is only available for the first 4 years of practice and will be presented in a Life Table Analysis.
It is important to bear in mind that the effectiveness of NPT improved over time as the physicians offering treatment gained greater experience and it is likely to be even more effective than present results would indicate. Also, a key factor in giving couples the best chance of success is for them to complete 12 effective cycles of treatment which can take from 18 to 24 months after beginning the program. Unfortunately many couples gave up prior to reaching this desired end point, largely because the goals of treatment were not clearly outlined by their physicians from the outset.

## STUDY GROUP

All patients with previously unsuccessful ART who conceived with NPT treatment through a Family Physician's practice in Galway, Ireland were included in this study, between 2nd Feb 1998 and 1st Feb 2004. 4 patients were excluded from the study because 2 were already pregnant at the initial medical consultation and a further 2 previously had a successful pregnancy with IVF prior to conceiving with NPT.
95 Patients conceived 123 times. The average female age per conception was 36.8 years, with a range from 28 to 47 years. The couples had been trying to conceive for an average of 6.1 years and had 176 failed attempts at ART, with 175 unsuccessful embryo Transfers. There was an average of 2 unsuccessful attempts at ART per couple. (See Table 1.)

**TABLE 1. Profile of ENTIRE GROUP - 95 Couples**

| | **Average** | **Range** | **Total** |
|---|---|---|---|
| **Female Age** | 36.8 years | 28 – 47 years | |
| **Years trying to conceive** | 6.1 years | 2 – 13 years | |
| **Attempts at ART** | 1.85 | 1 - 7 | 176 |
| **Attempts at Embryo Transfer** | 1.84 | 0 - 5 | 175 |

## RESULTS WITH NPT TREATMENT

There were 123 conceptions from 95 couples, resulting in 89 successful pregnancies from 74 of the couples. Fourteen out of the 74 couples had a second successful pregnancy and one had a third success with NPT. 21 of those who did conceive had a miscarriage (16) or ectopic pregnancy (4) as the final outcome. (Table 2.)
There were 3 twin pregnancies, giving a rate of 3.4% per live birth or 2.4% per conception.

**TABLE 2.**

| | |
|---|---|
| Total number of Conceptions | 123 |
| Total number of couples conceiving | 95 |
| Total number of Live Births | 89 |
| **Total number of couples with at least 1 Live Birth or ongoing pregnancy** | 74 |
| Total number with at least 2 Live Births | 14 |
| Total number with at least 3 Live Births | 1 |
| Total number of couples with ectopic / Miscarriage | **4 + 17 = 21** |
| Total number of twins | 3 |
| Twin Rate per live birth | **3/89 = 3.4%** |

A Life Table analysis shows the success rate of treatment from the first four years of practice. The figures for 6 years have not yet been calculated.

This table shows the adjusted proportion achieving pregnancy is 26.2% at 12 to 17 months, rising to 32.6% for 18 to 25 months in the program.

**TABLE 3…..Life Table**

**This Life Table shows the success rate of NPT following failed IVF for the first 4 years 1998-2002 incl.**

| Stage of Treatment | Number Starting in Event Category | Couples Withdrawing | | | Couples with Conceptions resulting in First Live Births or First Ongoing Pregnancies** | | | | Continuing treatment without live birth at end of study follow up | Final Outcome Misc or ectopic without live birth |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Number | Cumulative Number | Cumulative Crude Percentage of All Subjects | Number | Cumulative Number | Cumulative Crude Percentage of All Subjects | **Adjusted Proportion Achieving Pregnancy** | | |
| 0 - 2 months | **351** | **8** | 8 | 2.3% | **7** | 7 | 2.0% | 2.0% | **0** | **0** |
| 3 - 6 months | **336** | **72** | 80 | 22.8% | **17** | 24 | 6.8% | 7.6% | **0** | **5** |
| 7 - 11 months | **242** | **79** | 159 | 45.3% | **16** | 40 | 11.4% | 15.0% | **0** | **2** |
| 12 - 17 months | **145** | **62** | 221 | 62.9% | **15** | 55 | 15.7% | **26.2%** | **0** | **1** |
| 18 -25 months | **67** | **29** | 250 | 71.5% | **4** | 59 | 16.8% | **32.6%** | **11** | **2** |
| 26 - 36 months | **21** | **7** | 257 | 73.2% | **2** | 61 | 17.4% | 43.8% | **10** | **1** |
| > 36 months | **1** | **0** | 257 | 73.2% | **0** | 61 | 17.4% | 43.8% | **1** | **0** |
| **TOTAL NUMBERS** | **351** | **257** | | | **61** | | | | **22** | **11** |

## ANALYSIS OF PREGNANCIES

### ➢ Analysis of 95 Patients who conceived

The previous obstetrical history for the 95 couples who conceived is outlined in Table 4.
42 of the couples had never conceived naturally before. 29 did conceive, but never had a live birth and 24 couples had a previous live birth.
The average duration of Infertility was 6.1 years, with a range from 2 to 13 years. (Table 5.)
Females aged 33 years and younger account for only 15% (18/123) of conceptions, while those aged 40+years account for 21% (26/123). The majority of women were 34 to 39 years old, making up 64% (79/123) of conceptions. (Table 6.)

**TABLE 4. Obstetric History**

| | Nulligravida | Nulliparous | Secondary Infertility |
|---|---|---|---|
| Past Obstetric History | 42 (44%) | 29 (31%) | 24 (25%) |

**TABLE 5. Average duration of Infertility**

| Years Trying to Conceive | Number of Couples |
|---|---|
| ≤ 2 years | 4 |
| 3 years | 8 |
| 4 years | 13 |
| 5 years | 21 |
| 6 years | 19 |
| 7 years | 6 |
| 8 years | 9 |
| 9 years | 7 |
| 10 years | 1 |
| 11 years | 2 |
| 12 years | 4 |
| 13 years | 1 |

TOTAL = 95 Couples

**TABLE 6. Women's Age at Conception**

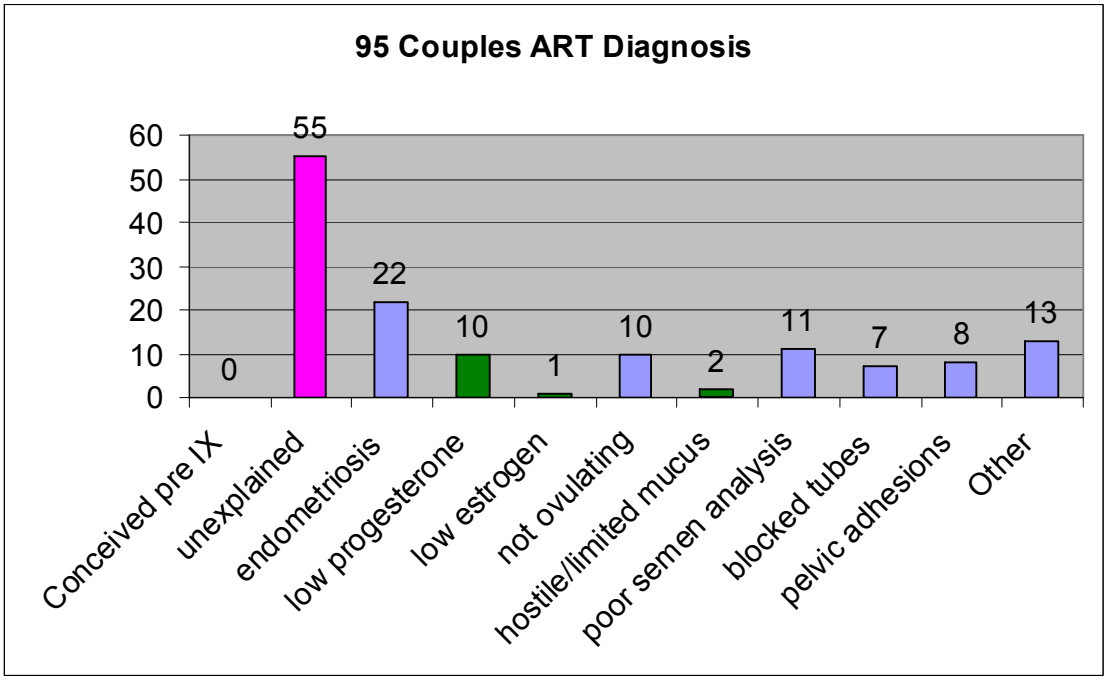
**123 conceptions from 95 couples with previous failed ART**

| Age (Years) | Number of Conceptions |
|---|---|
| ≤ 30 | 5 |
| 31-33 | 13 |
| 34-35 | 25 |
| 36-37 | 26 |
| 38-39 | 28 |
| 40-41 | 15 |
| 42-43 | 7 |
| 44+ | 4 |

Average Age = 36.8 years Total = 123

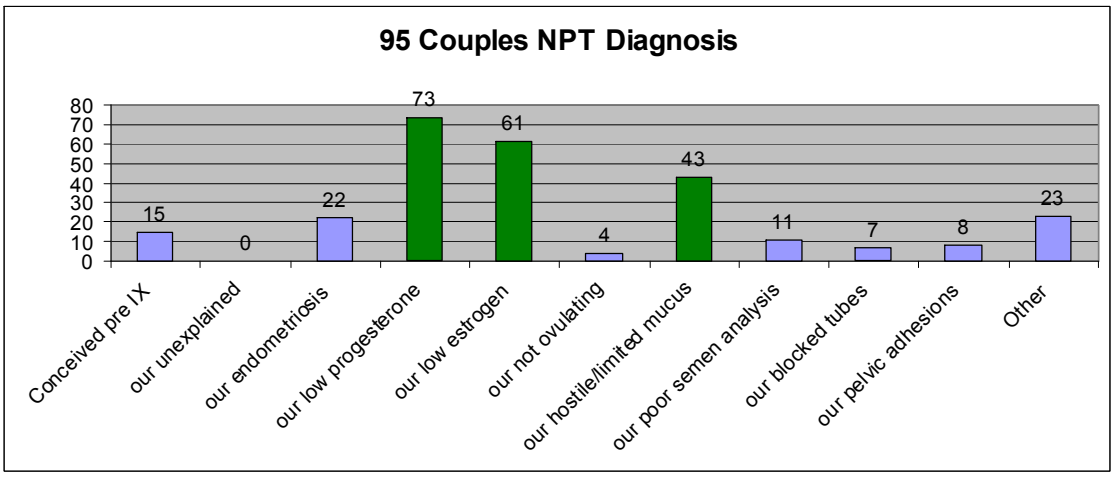
The profile of this group shows that fifty-five (58%) of the couples had an initial diagnosis of unexplained infertility (fig. 1). Twenty-two couples had endometriosis, ten had low Progesterone, ten were deemed not to be ovulating, eleven had an abnormal seminal fluid analysis, seven had at least one blocked fallopian tube, eight had pelvic adhesions and thirteen were in some other diagnostic category. The sum of diagnoses exceeds 95 as some couples had a combination of 2 or more diagnoses.

**FIG 1.**



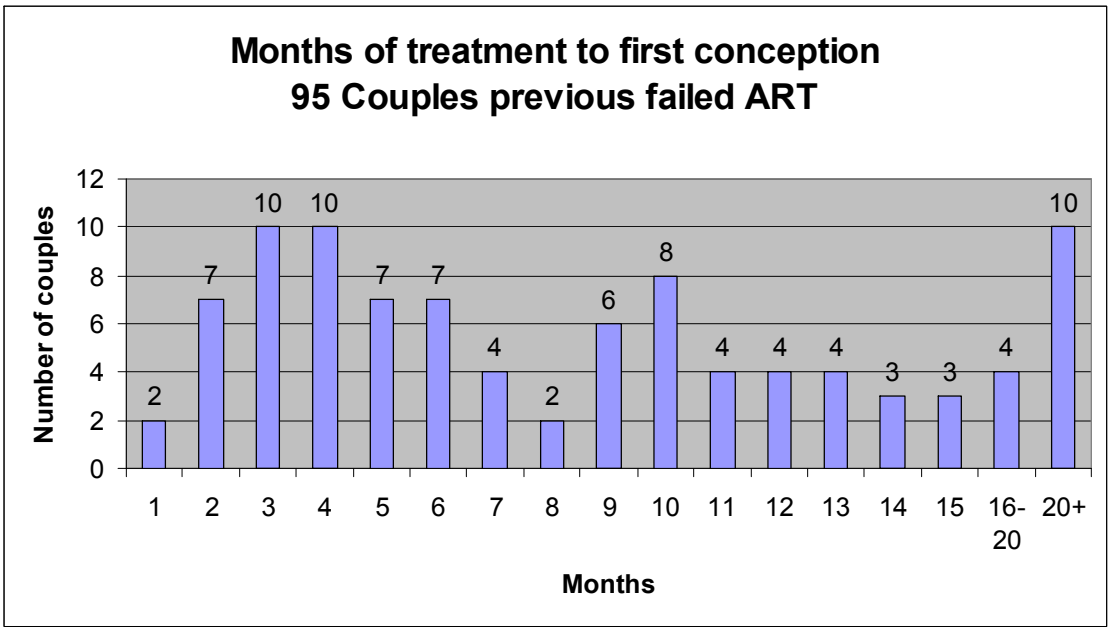

None of the couples had a diagnosis of unexplained infertility following NPT treatment. The principal differences with NPT diagnoses are the elimination of unexplained infertility and a large increase in the categories of low Progesterone, low Estradiol and unfavorable mucus. These hormone deficiencies were found because of the timed blood tests with respect to ovulation, which are more precise and therefore use a higher reference range than standard day 21 ranges. Estradiol measurements are usually not checked at all on day 21 in conventional fertility evaluation. Unfavorable mucus was identified with the Fertility*Care*™ Chart where cervical mucus scores were found to be below accepted normal ranges[4,5]. The rest of the diagnostic categories are largely unchanged except for a new column – Conceived pre-investigations. 15 couples actually conceived before investigations were completed, while they had just started tracking their signs of fertility. 10 of these 15 had a previous diagnosis of unexplained infertility.

**FIGURE 2.**




55% of couples conceived beyond 6 months into the program. 10 couples required more than 20 months before conception occurred. Some had taken a break for a time before resuming treatment, which was finally successful. Others had a delay in pursuing surgical evaluation and conceived when medical treatment was resumed following surgical intervention (Fig 3.) In general most couples have completed treatment by 24 months into the program.

**FIG. 3. Months of treatment before conception**

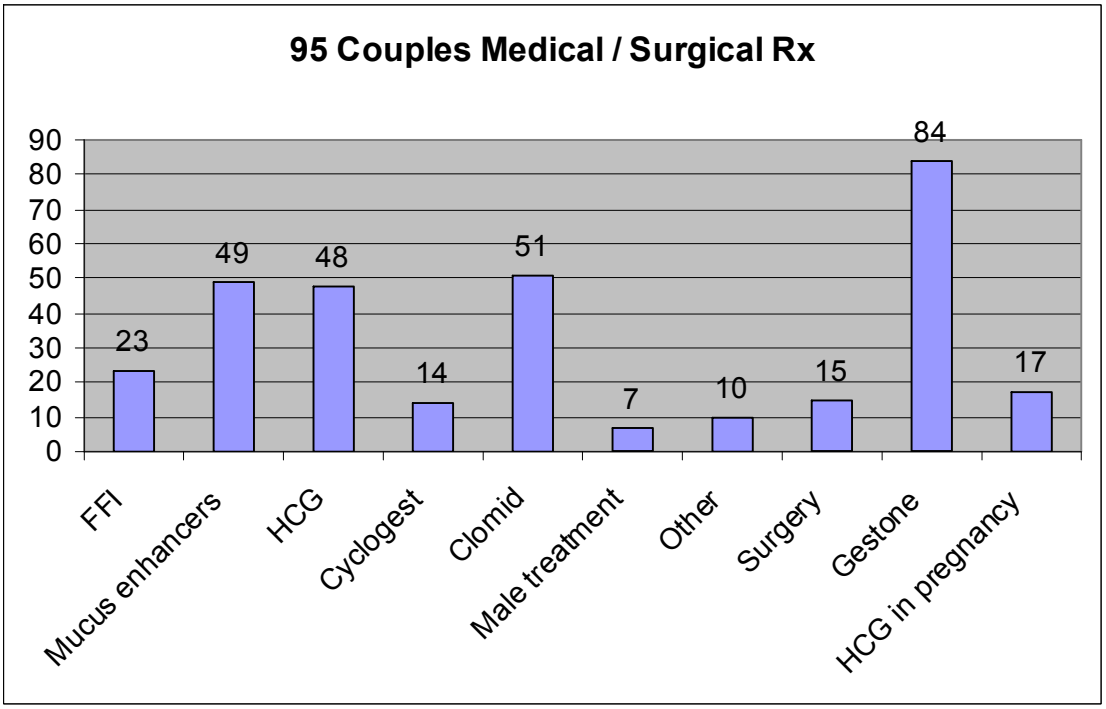


A summary of the treatment which couples received is outlined in figure 4. Couples often had a combination of different treatments, which is why the sum of medical interventions is greater than 95. Fifty-one women had ovulation induction with Clomiphene and forty-eight had a series of HCG injections 2000 units on days 3, 5, 7 and 9 after ovulation according to the fertility chart. Forty-nine had some form of mucus enhancing medications and ten couples had other medical treatment including Bromocryptine, Thyroxine and Ciclofenile (Neoclym). One couple with a diagnosis of hypothalamic amenorrhoea required treatment using a GNRH pump. They conceived on their 3rd cycle of pulsatile GNRH for their first NPT pregnancy.

Seven men required fertility treatment. Four had Tamoxifen, two had prednisolone and one had antibiotics, vitamin and mineral supplements. Fifteen women conceived following surgical interventions, 10 following diathermy of endometriosis, 2 post myomectomy, 1 post polypectomy and 2 had successful microsurgical reconstruction of blocked fallopian tubes.

During pregnancy 84 women had progesterone support and an additional 17 also had HCG to try and reduce the risk of miscarriage. This was usually recommended in cases of 2 or more previous miscarriages of if the hormone levels were found to be very low on the cycle of conception. 11 couples did not have any hormone support during pregnancy.

**Figure 4.**

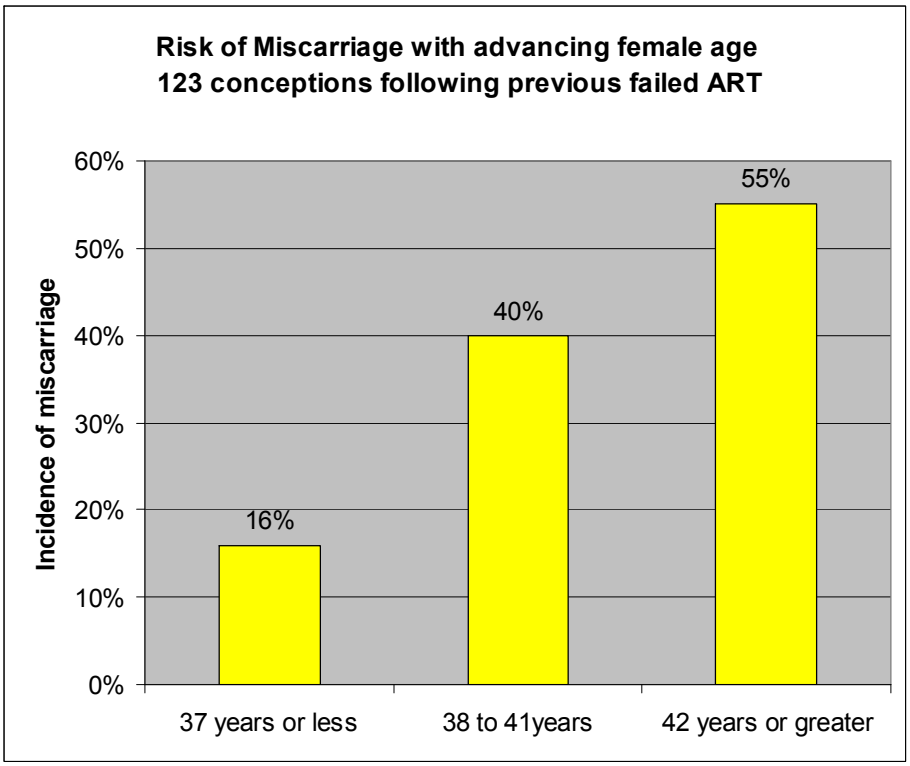


## ➢ Outcomes of all 123 conceptions

84% of those who conceived aged 37 years or less had a successful outcome, with 16% ending in miscarriage or ectopic pregnancy. But for women aged 38 years or greater, only 57.4% had a successful outcome, with a 42.6% risk of unsuccessful pregnancy. The risk of an adverse outcome was more than twice as high for older women. The overall risk of miscarriage or ectopic pregnancy for all age groups was 27.6% (Table 7). These figures are also plotted on a bar chart below to show the correlation of adverse pregnancy outcome with advancing female age. 55% of women aged 42 years or greater had an adverse outcome to their pregnancy.

**Table 7.**
**Pregnancy Outcomes from all 123 NPT conceptions from 95 couples with previously unsuccessful ART**

| | Number of conceptions | Live Births | Ongoing pregnancy | Successful Pregnancies | Total Adverse outcome | Miscarriage | Ectopic |
|---|---|---|---|---|---|---|---|
| **Age ≤ 37** | 69 | 53 | 5 | **58 (84.0%)** | **11 (16.0%)** | 8 (11.6%) | 3 (4.4%) |
| **Age ≥ 38** | 54 | 29 | 2 | **31 (57.4%)** | **23 (42.6%)** | 21 (38.9%) | 2 (3.7%) |
| **All Ages** | 123 | 82 | 7 | **89 (72.4%)** | **34 (27.6%)** | 29 (23.5%) | 5 (4.1%) |



## ➢ Outcomes for all 95 coupless

**Table 8.**
**FINAL Pregnancy Outcomes from all 95 NPT couples with previously unsuccessful ART**

| | 1 or more Live Births | Ongoing pregnancy | Successful Pregnancies | Total Adverse outcome | Miscarriage | Ectopic |
|---|---|---|---|---|---|---|
| **All 95 couples** | 69 | 5 | **74 (77.9 %)** | **21 (22.1%)** | 17 | 4 |
| **Average Age** | | | **36 Years** | **39 years** | | |

Looking at all 95 couples, some had a miscarriage on their first pregnancy, but subsequently went on to have a successful pregnancy on their second or third attempt. The final outcomes for the 95 couples show that 74 eventually had at least one successful "Take Home" baby and 21 did not. Fourteen of the 74 successful couples went on to have another successful pregnancy and one had a third success.

Finally, if we look at all of the couples with a history of previous failed ART between 1998 and 2002, it appears that a higher number of past IVF attempts is associated with a lower NPT live birth rate. This effect does not appear to be related to advancing female age. Although those with 3 and more previous attempts with ART are a little older, the average female age is still below 38 years. If a couple had one previous attempt at ART the NPT crude live birth rate was 28.9%. This fell to 18.4% with 2 previous ART attempts and was just 13.3% if there were 3 or more previous attempts with ART. (Table 8.)

**Table 8.**
**NPT Pregnancy success rates according to number of previous failed ART attempts, including all conceptions and all live births for 4 years 1998 -2002.**

| No. of IVF Attempts | Average Female age | Number of couples | Total Number of conceptions | Total number of Live Births or ongoing pregnancy | Crude Live Birth Rate |
|---|---|---|---|---|---|
| **1** | **36.5** | 82+5+34=121 | 47 | 35 | **28.9%** |
| **2** | **36.2** | 94+9+22=125 | 24 | 23 | **18.4%** |
| **3+** | **37.5** | 81+8+16=105 | 22 | 14 | **13.3%** |
| **All** | **36.7** | **351** | **93** | **72** | **20.5%** |

# DISCUSSION

There are many different ways to analyze the results of NPT fertility treatment, but whatever way we look at the figures we can confidently say that a significant number of couples will conceive with this approach. Everybody knows of dramatic stories about couples that had been trying to conceive for years without success, who spontaneously achieve a pregnancy after

finishing with fertility treatment or following a successful adoption. Clinical consensus is that about 5% of couples with failed IVF will conceive subsequently without any intervention. For the first 4 years of treatment (1998-2002), we have a success rate of up to 32.6% or more depending on how we interpret the results of NPT treatment. 12 couples within this group conceived with fertility focused intercourse alone without medical treatment. This represents a success rate of 3.4%, which is comparable to the expected spontaneous pregnancy rate eventually following failed IVF. We have observed that the process of learning how to track the biologic markers of fertility leads to couple empowerment, stress reduction and often to restoration of normal reproductive function. This is especially the case where couples have been under a lot of stress prior to commencing NPT. There is a temptation to count pregnancies which have occurred prior to the introduction of medical treatment as "non-NPT pregnancies", however the process of fertility tracking itself is an intervention, central to our program, which improves pregnancy rates even in the absence of medications. Most couples who did conceive in this way also had progesterone support[10,11] usually for 12 to 16 weeks gestation in an attempt to reduce the risk of subsequent miscarriage.

This group of patients had reached the end of available conventional infertility treatment options, including ART but had not yet tried NPT. Despite advanced female age, long-standing infertility and previous unsuccessful attempts with ART we still achieved a remarkable 32.6% success rate with NPT treatment. Increasing numbers of past IVF attempts were associated with decreasing live birth rates with NPT treatment. This cannot be accounted for simply because of advancing female age, and one must suspect that the process of ART itself may have an adverse effect on the couple's fertility potential, making future pregnancies less likely. We feel it is crucial for couples to consider NPT before ART, especially because of the possible negative impact of ART against future NPT success. However, as the above figures show, NPT can still be effective, even after multiple failed attempts at IVF.

NPT aims to find out why couples cannot conceive and then tries to correct the identified abnormalities – hormone deficiency, unfavorable mucus, anovulation, endometriosis, male factor……etc. When a functional or structural abnormality is identified and corrected we expect a restoration of normal reproductive function. It is interesting to look at our group of 95 couples who did conceive and compare the diagnoses pre and post NPT evaluation. We had a dramatic increase in the categories of low progesterone, low estradiol and unfavorable mucus. The group of unexplained infertility was practically eliminated. This reflects a shortcoming in the present evaluation process for couples with infertility. The timed hormonal blood tests for both progesterone and estradiol[5] help us to identify subtle deficiencies that are simply not diagnosed with a day 21 blood test that does not pay any attention to the time of ovulation. In addition the Creighton Model Fertility*Care*™ System can diagnose abnormal mucus flow and abnormal bleeding patterns that otherwise pass unnoticed.

The surgical interventions are worth emphasizing as well. Many couples with a diagnosis of endometriosis have not had effective surgery to correct this. We have had some couples, who were originally deemed to have a normal pelvis following laparoscopy and dye test. A second look laparoscopy through our program, following referral to a known skilled gynecologist frequently found previously undiagnosed endometriosis. Adequate detection and removal of endometriosis improves fertility rates[6]. Furthermore we have had two live births following

myomectomy[7]. The fibroids were previously deemed insignificant by the ART specialist, but in the opinion of a micro-surgeon they were regarded as problematic and subsequently removed, restoring normal fertility. It is important for NPT Physicians to have access to skilled co-operative surgeons to maximize the chances of successful treatment.

If a couple did achieve fertilization with NPT, the probability of successful maintenance of implantation was 72.4% for all age groups. Women aged 37 years or younger had an 84% probability of successful pregnancy if they managed to conceive. Remember this is a population of patients where most of them did achieve successful fertilization previously with ART, but the embryos failed to implant in all of them. Embryo wastage and failed implantation is generally accepted by the medical community to be very high in the normally fertile population[8]. It is often stated that implantation success rates from IVF cycles are comparable to what occurs in nature. These data would contradict that assumption. Clearly the vast majority of embryos, resulting from NPT successfully implanted and concluded with a live birth, especially in younger women. The higher probability of miscarriage in the older women is most likely related to an increased incidence of embryonic developmental abnormalities which were incompatible with life[9]. Hormone support with progesterone and HCG may also have played a significant role in reducing the risk of miscarriage for these patients[10,11].

Achieving a live birth is not the only parameter by which we judge successful treatment with NPT. Couples are clearly informed at the outset that they may not succeed, but we do want to give them the best chance possible before reaching the end of the program. While every effort will be made to help each couple to conceive, we do not want to reach this goal at the expense of their health, their sanity or relationship. Many couples report feeling healthier and say that NPT has helped them to accept involuntary childlessness in a way which ART could never do. Restoration of gynecologic health and a strengthening of the relationship are also successful outcomes which have not been measured in the figures reported. This is the experience for the majority of couples and makes the process a rewarding and fulfilling one for the physician and patients alike. Adoption is also viewed as a very positive outcome for the couple if it is not possible for them to have a child of their own.

NPT pregnancies are very different from ART pregnancies in many respects. The immediate and most striking difference is that we have a very low incidence of twins, and in the Irish program have not yet had triplets. The incidence of multiple births is just 3.4%, compared with a multiple birth rate of 1.2% without fertility treatment, 9% with clomiphene in general use and an average of 53% for ART programs in the USA[12]. Multiple births are more prone to prematurity, which increases the incidence of complications such as cerebral palsy, respiratory and gastro-intestinal problems. Premature delivery often results in a prolonged stay in the Special Care Baby Unit to deal with the newborn's medical problems[13]. Obviously this places an increased burden on hospital resources as treatment can be prolonged and expensive. NPT can significantly reduce these problems.

Another striking difference with NPT is that once a couple have had a successful pregnancy, their chances of subsequent successful pregnancies are excellent. NPT is a corrective treatment which restores normal reproductive function. Having identified and corrected the abnormality which previously prevented a successful pregnancy, future pregnancies occur quite easily in

most cases. A minority of couples will not conceive again, usually due to advancing female age, but most will be succeed with future attempts. Fourteen of our couples did have a second successful pregnancy and one of them even had a third success. One would expect this figure to increase further with time as more couples return for another attempt. This is not the case with ART which is circumventive and not corrective in nature. Infertile couples generally remain infertile, even after they have had a successful IVF pregnancy[14].

## CONCLUSION

Remarkably, 42% of couples who attempted IVF in the UK in 1998-1999 had a diagnosis of unexplained infertility[2]. This must call into question conventional infertility evaluation protocols. How is it possible with all of the recent advances in modern medicine that this aspect of health is so poorly understood? Obviously something is preventing these 42% of couples from conceiving – but this something is not found with current diagnostic techniques.

It is likely that a significant number of previously unexplained infertile couples may have subtle hormonal or mucus abnormalities which can be detected using the Creighton Model Fertility*Care* System and NPT techniques. Identifying these abnormalities will surely lead to establishing a diagnosis for infertility in more cases. When medical and surgical interventions are applied in co-operation with a system which empowers the couple through education and stress management, higher pregnancy rates do occur, especially if treatment is extended over a two-year period of time.

Evidence is accumulating in favor of NPT as the method of choice in promoting fertility awareness, maintaining gynecologic health and treating couples with infertility and recurrent miscarriage. It is an uncomplicated common sense approach to understand and treat nearly every cause of infertility. This chapter has shown the effectiveness of NPT, even in cases of long standing infertility, advanced female age and previous failed attempts at IVF. The tragedy in medicine today is that physicians often adopt high-tech, invasive approaches without adequately investigating underlying pathophysiologic causes, and simpler treatment options for infertility.

Doctors need to learn how to think again! Remember how to be a physician that uses your medical knowledge as a means of applying new approaches in a sensible manner. As the old latin dictum goes “Primum non nocere – First do no harm!” Most of the medications used in NPT are currently used in many infertility programs. NPT differs primarily in the way this treatment is applied with respect to the CrMFCS in a methodical and measured fashion to restore normal reproductive function. Trying to apply these treatments without using the Fertility*Care*™ System is worse than trying to find your way around a new city without a map…..you simply get lost!

The NPT approach is new and exciting. This chapter provides evidence that NPT is superior to conventional medical approaches in the area of infertility. It questions current practice when a relatively simple, minimally invasive, family physician based program can help 95 couples to achieve 89 successful pregnancies despite a history of previously failed ART.

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