

# An Integrated Approach to Male-Factor Subfertility: Bridging the Gap Between Fertility Specialists Trained in Urology and Gynaecology

Edward G. Hughes, MB ChB,<sup>1,2</sup> John Grantmyre, MD,<sup>3</sup> Armand Zini, MD<sup>4</sup>

<sup>1</sup>ONE Fertility, Burlington ON

<sup>2</sup>Department of Obstetrics and Gynecology, McMaster University, Hamilton ON

<sup>3</sup>Department of Urology, Dalhousie University, Halifax NS

<sup>4</sup>Department of Surgery, McGill University, Montreal QC

## Abstract

Subfertile men and women are usually cared for by different clinicians, namely urologists and gynaecologists. While these doctors share each other's goals, they may not always appreciate the content or implications of their opposite number's clinical decisions; to some degree they may practice in "silos." We address this problem by reviewing the effectiveness of medical treatments for male factor subfertility in the context of female factors. The effectiveness of treatments for couples with male factor subfertility, other than IVF with ICSI, appears modest. However, data from randomized controlled trials suggest benefits from some treatments: clomiphene and tamoxifen for the male (common odds ratio for pregnancy [COR] 2.42; 95% CI 1.47 to 3.94), antioxidants (COR 4.18; 95% CI 2.65 to 6.59) and surgical management of a clinical varicocele (COR 2.39; 95% CI 1.56 to 3.66). Nevertheless, close attention to female age and the duration of subfertility help to avoid lost opportunity through delays in treatment when IVF with ICSI is indicated. Making treatment decisions squarely in the context of the couple's overall prognosis is key for optimal outcomes. Future trials of male fertility treatments should focus on pregnancy as the primary outcome, rather than less important surrogates such as sperm quality.

## Résumé

Les hommes et les femmes hypofertiles obtiennent habituellement leurs soins auprès de cliniciens distincts, soit des urologues et des gynécologues, respectivement. Bien que ces professionnels de la santé aient des objectifs communs, il est possible qu'ils ne comprennent pas toujours le contenu ou les implications des décisions cliniques de leurs homologues; on pourrait même en venir à affirmer qu'ils agissent de façon cloisonnée. Nous traitons de ce problème en analysant l'efficacité des traitements médicaux visant l'hypofertilité masculine dans le contexte des facteurs féminins. À l'exception de l'utilisation concomitante de la FIV et de l'ICSI, l'efficacité des traitements offerts aux couples qui font face à une hypofertilité attribuable à des causes imputables à l'homme semble modeste. Toutefois, des données issues d'essais comparatifs randomisés semblent indiquer que certains traitements offrent des avantages : clomiphène et tamoxifène administrés à l'homme (rapport de cotes commun pour ce qui est de la grossesse [RCC], 2,42; IC à 95 %, 1,47 - 3,94), antioxydants (RCC, 4,18; IC à 95 %, 2,65 - 6,59) et prise en charge chirurgicale d'une varicocèle clinique (RCC, 2,39; IC à 95 %, 1,56 - 3,66). Quoiqu'il en soit, le fait de bien porter attention à l'âge de la femme et à la durée de l'hypofertilité aide à éviter les occasions manquées en raison de délais dans la mise en œuvre du traitement, dans les cas où l'utilisation concomitante de la FIV et de l'ICSI s'avère indiquée. Le fait de prendre des décisions en s'assurant de tenir absolument compte du pronostic global du couple est d'une importance capitale pour l'obtention d'issues optimales. L'obtention d'une grossesse (et non des critères auxiliaires moins importants, tels que la qualité des spermatozoïdes) devrait constituer le critère d'évaluation principal des futurs essais visant les traitements contre l'infertilité masculine.

**Key Words:** Male infertility, female infertility, patient-centered care, integrated care, fertility trials, varicocele, anti-oxidants, anti-estrogens

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## INTRODUCTION

An ancient fable tells of six blind men from a small village, who upon meeting an elephant, are able to perceive the beast only from their own marginal perspectives. “It’s a rope” cries the man holding the tail, while his friend embracing the leg calls out “it’s a tree.” As gynaecologists and urologists caring for couples with male factor subfertility, we run the risk of seeing clinical problems in a similarly narrow way. Couples seeking our help want an integrated approach, not a disparate one. They want rapid, effective, safe, and affordable solutions, and while they may also seek answers to the question “what is causing this delay?” their primary goal is a healthy live birth as simply and quickly as possible. How can we best provide a seamless and effective response to this need when the current model for care involves two different clinicians caring separately for male and female partners?

Urologists have become important members of teams providing fertility care, but they usually provide such care as an adjunct to their general urology practices. In Canada, many have not undergone formal subspecialty training in andrology, because there are only two andrology fellowship programs available. Also, they may see male fertility patients in offices that are geographically remote from the rest of the team, and may even see men separate from their female partners. On the other hand, gynaecologic reproductive endocrinology and infertility specialists may have become overly focused on their female patients. Many modern assisted reproductive technology clinics began as gynaecology offices, and although they may have expanded into complex multidisciplinary teams, they often remain under the medical leadership of their founding gynaecologists. Again, they may pay less attention to male factors than they should.

Clearly, both specialty groups have a responsibility to communicate and collaborate effectively within this structure. Our goal here is to review subfertility care for couples with a male factor, from both male and female care perspectives. We focus on the key elements of care that the parallel physician may not fully appreciate but needs to acknowledge. In particular, a better understanding of the effectiveness of andrology care may encourage more

appropriate and timely referral to the urologist. Conversely, a clear vision of the powerfully negative impact of advancing female age and duration of subfertility on outcome may prevent patients from being sidetracked down male and/or female treatment avenues that are short on success but long on time commitment.<sup>1-3</sup> We hope that we will persuade gynaecology and urology specialists to increase their awareness of each other’s challenges and thus be better positioned to provide effective care for subfertile couples dealing with abnormal sperm quality.

## AN OVERVIEW OF SUBFERTILITY PROGNOSIS, WITH AND WITHOUT TREATMENT

Paradoxically, the issue central to appropriate fertility treatment choice, for male and female partners, is a clear understanding of prognosis for live birth without treatment. Paying close attention to a couple’s baseline prognosis reduces the risk that they will neither enter treatment too soon nor run out of time while pursuing male or female treatment options of marginal value.

There are many robust data sets that inform the question of treatment-independent prognosis in subfertility.<sup>1-3</sup> Scoring systems derived from these reports are widely used in Europe to direct public health policy. In the Netherlands, for example, where fertility care including ART is publicly funded, national guidelines dictate that couples with a 40% chance of treatment-independent pregnancy should wait another year before using therapy.<sup>4</sup> Here are three clinical scenarios that illustrate the powerful effects of female age and duration of trying to conceive on outcome:

- A 28-year-old woman whose partner’s sperm shows a significant reduction to 20% total motility (normally > 40%), but in whom the duration of unprotected intercourse has been only 12 months, has a 40% probability of treatment-independent pregnancy over the following 12 months. In the Netherlands, this couple would thus be advised to defer treatment for another 12 months.
- Conversely, a 28-year-old woman with two years of primary subfertility, and a partner whose sperm have the same low motility of 20%, has an estimated chance of spontaneously conceiving within 12 months of 20%. This would trigger a recommendation for intrauterine insemination followed by in vitro fertilization with intracytoplasmic sperm injection if unsuccessful.
- Finally, a 35-year-old woman with the same scenario, but of three years’ duration, in whom the prognosis falls to 10% in the subsequent year, would be better advised to move more quickly to IVF with ICSI.

## ABBREVIATIONS

ART	assisted reproductive technology
COR	common odds ratio
IUI	intrauterine insemination
NNT	number needed to treat
REI	reproductive endocrinology and infertility

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