in the training of the clinicians treating infertile patients for whom clinical andrology must now become an important part of their curriculum.

Clinicians undertaking the treatment of infertility must therefore now undertake a wide area of training. The curriculum must involve a great deal of basic physiology, gynaecology and urology. These practitioners must be able to examine both male and female patients competently and recognize pathologies in either partner where they exist. The clinicians must also be taught semenology and of course all the practical aspects of reproductive technology.

The treatment of infertility must, in our view, no longer be the preserve of gynaecology. In many countries, including Australia, the subspeciality examinations in infertility and reproductive endocrinology appear to relate solely to the female patient. Scant attention seems to be given, at least in the published curricula of such examinations, for any aspect of male infertility except that which relates to the examination of semen and its manipulation within an IVF laboratory. This state of affairs is greatly in need of change. In our view, such a subspeciality examination needs to be removed from the over-riding influence of the Obstetric and Gynaecological Colleges if only to emphasize that infertility is a male as well as a female problem and also to facilitate the inclusion of the urologists into this sphere of therapy.

We would thus like to see the same changes made to the training of clinicians involved in the management of infertility. Firstly, all clinicians treating infertile couples should have training in both urology and gynaecology. Gynaecologists wishing to subspecialize in infertility should have a minimum of one year in full time urology and the urologists should spend the same length of time in gynaecology. This should be a standard requirement for anyone claiming to be a subspecialist in this area. Both urologists and gynaecologists should have training in the clinical as well as the laboratory aspects of reproductive technology, semen handling, semen analysis and sperm and embryo storage as well as the laboratory techniques involved in embryo manipulation. Infertility should now be a subject set aside from either urology or gynaecology thus allowing the two specialties to come together, at long last.

We believe that the next decade will be a very important time for clinical andrology: either we will come to understand the patho-physiology of the genital tract, or reproductive technology will become so successful that we will not bother to find out. If the former comes to pass there may be many ways in which we can prevent the disorders collectively known as male infertility and avoid the need for treatment altogether. If the latter occurs, then prevention will be forgotten and all infertility will be treated by assisted conception with all the problems that it may give future generations (Cummins and Jequier, 1994).

The choice between these two options by the infertile patients is likely to be obvious.

References


Declining clinical andrology: fact or fiction?*

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The debate initiated by Jequier and Cummins (1997) provides an excellent basis for an evaluation of the current status of the clinical investigation of the aetiology of male infertility. In their paper, the authors express their concern about the negative impact of intracytoplasmic sperm injection (ICSI) on the clinical investigation of male infertility.

For years, male infertility has been an area of frustration. Despite the growing knowledge on spermatogenesis and sperm function thanks to advances in both cell biology and molecular biology, there has been hardly any substantial advance in the treatment of male infertility. Indeed, any ‘clinician attempting to deal with male infertility is constantly reminded of the lack of detailed understanding of the pathophysiology of defects in spermatogenesis and spermiation which appear to underlie the disorders seen in the majority of the patients’ (Baker, 1993). For many years, this discrepancy between our basic knowledge of mechanisms leading to male infertility and their treatment has resulted in the dissemination of so-called empirical treatments (Belaïsch, 1993). Although still widely applied, most of these treatments are assumed to be ineffectual

*Partially based on an internet-published paper on http://ferti.net, where all commentaries on the present paper may be posted.
and it is only assisted reproductive technology (ART) which offers interesting perspectives for the treatment of unexplained male infertility (O’Donovan et al., 1993). In recent years, most efforts in ART, a body of technologies emerging from cooperation between gynaecologists and reproductive scientists, have focused on the enhancement of the in-vitro fertilization (IVF) process. Although the basic physiology of normal fertilization still remains poorly understood, these efforts led ultimately to the first successes with ICSI (Palermo et al., 1992).

Since the introduction of ICSI, the clinician dealing with the infertile male has access to a powerful tool for alleviating male infertility. By means of ICSI, fertilization and pregnancies can be obtained successfully with spermatozoa recovered or from an ejaculate, or from the epididymis either from the seminiferous tubules irrespective of whether spermatogenesis is normal or deficient and irrespective of whether the underlying pathophysiology is understood or not. ICSI is thus rapidly becoming a routine treatment for all reproductive clinicians dealing with male infertility. Nowadays this treatment is certainly not the exclusive province of gynaecologists alone.

But the magic of ICSI may also put a spell on the infertile patient who is less interested in the pathophysiology of his problem than in having his own child as quickly as possible. In the near future cost–benefit analysis and the utilitarianism often associated with ‘evidence-based medicine’ may also provide a reason for health authorities to support ICSI as a treatment of long-standing male infertility rather than to support basic research aimed at understanding its pathophysiology. Thus long-standing male infertility, although remaining an ill-defined condition, may become a trivial issue with a simple cost-effective approach bypassing any detailed diagnostic work, i.e. ICSI.

The risk of a disease as described by Jequier and Cummins (1997) may exist. Worse, it may eventually reach epidemic proportions, probably not because of the utilitarianism of ART clinicians but rather because of patients’ attitudes towards their own infertility and because authorities are focusing on short-term health policies.

But what about the cure?
The ultimate desire of the couple experiencing infertility is the wife’s pregnancy. Traditionally, the female has been considered the prime cause of barren marriages. It is for this reason that the gynaecologist is often the first fertility specialist to enter the field. Accurate assessment of the female factor is very important even in male subfertility. Indeed, male and female subfertility are known to be closely interrelated. Many couples where the male partner may be subfertile will probably never seek medical help because the female partner fully compensates for the ‘male factor’, resulting in no delay in conception. Conversely, a male partner may be judged to have a problem while in fact the couple’s fertility status may be negatively influenced by a concurrent and even more important problem in the female. The diagnosis of male subfertility can obviously only be made after an appropriate assessment of the ‘female factor’.

To cope with this particular situation, Jequier and Cummins suggest a change in attitude involving at least a joint clinical approach by both an urologist and a gynaecologist or, even better, a change in the training of the reproductive clinician dealing with male infertility, i.e. the reproductive andrologist. Neither their plea for a change nor their proposal is new (Jequier, 1990). Any gynaecologist or urologist involved in male infertility should acquire minimal theoretical and practical skills in investigating and treating disorders of the genito-urinary tract of either sex. Whether this change may prevent the ‘decline’ in clinical andrological investigation is questionable.

Indeed, proper training in urology or gynaecology or even both is certainly not a guarantee of good medical practice and many examples of the ‘decline’ in male clinical andrology are, in fact, just examples of poor medical practice. A recent letter in this journal (Canale and Caietti, 1996) illustrates that permanent re-training should be compulsory and may be more effective in preventing poor medical practice in clinical andrology than the fact of whether the clinician was originally trained as a gynaecologist, urologist, endocrinologist or dermatologist.

A training programme for a clinical reproductive andrologist should perhaps not be limited to a full or partial training in urology and gynaecology alone. Practical skills or theoretical understandings in the male infertility clinic may be unfamiliar in either of the two disciplines, e.g. electroejaculation, genetics. It may therefore be preferable to set out minimum standards for the practical and theoretical skills which a reproductive andrologist should have or acquire, including principles from reproductive endocrinology, clinical genetics, embryology and microsurgery. In Europe, the European Academy of Andrology is trying to set up such standards and to approve male infertility clinics with a broad multidisciplinary set-up for training in reproductive andrology (Nieschlag, 1996).

Secondly, we may ask whether the current standards for the evaluation of the male partner are sufficiently relevant to prevent a further decline in clinical andrology. Through a concerted action involving urologists, endocrinologists and gynaecologists, the World Health Organization (WHO) has set standards for the investigation of the infertile couple. For the male, these standards were first published as a supplement to The International Journal of Andrology (Comhaire et al., 1987) and were later incorporated without substantial modifications in a WHO manual (Rowe et al., 1993). This WHO standardized investigation is now becoming generally accepted as the gold standard for investigating the male partner (Comhaire, 1995).

The investigation consists mainly of history taking, physical examination, semen analysis, laboratory investigations and additional technical investigations. But will this investigation eventually provide an improvement in the understanding, the treatment and the prevention of male infertility?

History taking is an important key since ‘it will contribute to the diagnosis in one fourth of cases’ (Rowe et al., 1993). Indeed, history taking may provide many keys to diagnostic categorization. History taking, as suggested in the manual, will provide many keys to ‘damage-done-conditions’, e.g. mumps orchitis, cryptorchidism, chemotherapy. Only few keys will refer to conditions that are amenable, e.g. sexually transmitted disease or vasectomy where microsurgery may be
of some help, delayed puberty which raises the possibility of hypogonadotrophic hypogonadism or a misuse of anabolic steroids leading to spermatogenic depression.

The physical and andrological examination, again, may also provide many keys to ‘damage-done-conditions’, e.g. small testicular volume, but may also provide some keys to ‘conditions-under-debate’, e.g. varicocele or male accessory gland infection (MAGI). Again, only a few keys may refer to amenable conditions, i.e. epididymal swelling which might be related to an obstruction, small and soft testes which may be related to hypogonadotrophic hypogonadism, or scrotal swelling which might be indicative of testicular malignancy. If we look at the additional tests, again, many tests will refer only to non-manageable conditions. Endocrine testing including follicle stimulating hormone (FSH) and testosterone may be the key to the curable condition of hypogonadotrophic hypogonadism. Hyperprolactinemia may be associated with sexual dysfunction. But a screening blood analysis, anti-chlamydia antibodies and urine analysis may be only weak indicators for manageable conditions. As for the other additional tests, their efficiency in diagnosing causes of male infertility has never been properly assessed. Additional investigations such as thermography or ultrasound combined with Doppler may again be keys to ‘conditions-under-debate’ such as varicocele. While the incidence of testicular cancer may be increasing and may be closely related to male infertility (Carlsen et al., 1995), the WHO manual does not advocate any screening for testicular malignancies. Testicular biopsy is indicated only if both testicular volume and serum FSH concentrations are normal.

So far, it looks as if the ‘WHO standardized investigation’ may be a key to only a few amenable conditions which are currently not under debate: mainly infertility related to hypogonadotrophic hypogonadism, a rather infrequent problem with an incidence of ~1 in 3500 (Comhaire et al., 1987), or obstructions of the male genito–urinary tract. The impact of the ‘WHO standardized investigation’ on the treatment of male infertility by methods with a proven benefit may therefore be rather limited. Its direct impact on understanding the pathophysiology of male infertility may be even more limited. Making a final diagnosis of ‘idiopathic teratozoospermia’ by rigorously applying the WHO’s ‘objective criteria’ will probably not contribute to our understanding of the underlying pathophysiology.

Yet this standardized investigation has some merits and indirect benefits. It may allow a proper selection of patients who may benefit from specific, i.e. non-empirical treatments. For sure, any treatment or even cure which may obviate the need for ART is certainly more than welcome. The WHO categorization, although not helpful at all in providing any accurate prognosis for the infertile couple, may constitute a criterion to allow a better selection of infertile male subpopulations for further clinical or fundamental research into male infertility. Finally, the history-taking and clinical examination can easily establish a reassuring basis for subsequent counseling of the couple. One of the co-authors of the manual evaluated the impact of a WHO-like standardized investigation in more than 1000 couples attending a male infertility clinic and concluded that basically it did not improve the chance of fertility but mainly provided an opportunity for supportive counselling (Hargrave et al., 1986).

There is obviously an urgent need to redefine the standard investigation of male infertility since ICSI was introduced. ICSI has created many new opportunities to treat patients suffering from unexplained severe male infertility who at present cannot benefit from any specific or efficient treatment. But ICSI has also raised many new concerns (Cummins and Jequier, 1995; Cummins, 1997), many of which can be dealt with only by an accurate clinical work-up (Tournaye and Van Steirteghem, 1997). For this, new standards for andrological investigation should preferably originate from sound clinical evidence and should include updated tests based on actual insights into both the genetics and the epidemiology of male infertility. At present, investigations for deletions associated with cystic fibrosis (Jarvi et al., 1995; van der Ven et al., 1996) or spermatogenic failure (Kent-First et al., 1996) may be more important in terms of prevention of infertility and understanding the pathophysiology of male infertility than screening for subclinical varicoceles. Screening for testicular carcinoma-in-situ in subfertile men with a history of cryptorchidism may also be more important than screening for an ill-defined and debatable condition like subclinical MAGI. It is therefore questionable whether the ‘WHO standardized investigation’ still represents the ‘gold standard’ for investigation of the male partner in the era of ICSI.

In the next decade we should not only reorganize the training of the reproductive andrologist and be vigilant in keeping good clinical practice on the right track, but we must definitely set new standards for the clinical investigation of the infertile male. Only then can a clinician provide a satisfactory basis for further research into the pathophysiology and prevention of male infertility. Even the reproductive andrologist who has chosen to fight the good fight against the raiders of male fertility, may become impotent without a suitable weapon!

**References**


Clinical andrology is important for treatment of male infertility with ICSI

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In-vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI) has become the most important method of treatment for most forms of male infertility. Because of its high success rate the spectrum of indications has been continuously expanded from severe forms of male infertility to moderate or even mild reductions of sperm quality. Some infertility experts even suggest performing only ICSI for all forms of male infertility because of the reduced pregnancy rates with conservative and surgical treatment, intrauterine insemination (IUI) or IVF compared with ICSI. Therefore, in many IVF programmes male infertility patients are often referred to ICSI treatment very quickly, sometimes even without a sufficient diagnostic andrological work-up. This attitude creates two problems: firstly, with regard to the quality of medical practice (good medical practice), and secondly, the quality and progress of scientific knowledge (research into male infertility).

With regard to the first point, clinical evaluation of every male infertility patient’s clinical history, physical examination, repeated semen analysis and, based on these findings, additional microbiological, endocrinological and immunological examinations, are necessary. We should never forget that the worst possible situation for a patient, and certainly also for the physician, is reduced male infertility due to a testicular malignancy which remains undetected. Furthermore, despite the limited success rate of conventional treatment, it is our own experience that in several cases sperm quality or spermatogenesis can be improved by antibiotic, anti-inflammatory or immunological treatments and, following this, some potential cases of testicular sperm extraction (TESE) can be treated with the less invasive form of treatment by ICSI with spermatozoa retrieved from the ejaculate.

Secondly, a complete careful evaluation of the male patient, including history (medical, social, environmental), physical examination and evaluation of semen quality or spermatogenesis (e.g. testicular biopsy) are important requirements for identification of the aetiology of male infertility. Furthermore, it creates a valuable clinical basis for further scientific approaches to discover the pathophysiology of male infertility which consequently may open new approaches regarding prevention and treatment.

In summary, quality standards regarding treatment of male infertility have to include an appropriate diagnostic evaluation of the male by a physician specifically and sufficiently trained in andrology and reproductive medicine. ICSI is not a substitute for the andrologist, on the contrary, ICSI requires an andrologist. ICSI has opened a new field in clinical practice and research regarding treatment of male infertility as well as improving our understanding of sperm function and spermatogenesis which unfortunately has been so poor in the past.

Molecular biology in the modern work-up of the infertile male: the time to recognize the need for andrologists

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In a few months the reproductive scientific community will be celebrating the 20th anniversary of the first in-vitro fertilization (IVF) baby and, at the last census, it was calculated that some 1 500 000 births have occurred worldwide through the use of various assisted reproduction techniques (Olivennes et al., 1997). Taken as an isolated entity, this number is extremely satisfactory and it demonstrates that the establishment and practice of IVF and its associated technologies has been successful. Over the years, a number of breakthroughs have contributed to improve the overall success of these technologies. These include variations in protocols of ovulation induction, better in-vitro culture methods and more refined media, effective embryo cryopreservation and intracytoplasmic sperm injection (ICSI), to name just a few. Since the advent of ICSI, some 1500 births with close follow-up have been reported (Palermo et al., 1996; Tournaye and Van Steirteghem 1997); reassuringly, the frequency of major and minor congenital abnormalities in children conceived through ICSI (2.6% of births) is within the range observed with standard IVF.