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National Health Service provision for the management of infertility: the case for funding and reorganization of fertility services in the UK

Produced by a Multidisciplinary Working Party of the British Fertility Society, National Infertility Awareness Campaign and CHILD, the National Infertility Support Network: Laurence M. A. Shaw (Chairman)[1], Adam Balen[2], Elizabeth Lenton[3], Clare Brown[4] and Berkeley Greenwood[5]

[1]*Consultant Gynaecologist, East Kent Hospitals NHS Trust, Canterbury, Kent CT1 3NG, UK;* [2]*Consultant Gynaecologist, General Infirmary, Leeds LS2 9NS, UK;* [3]*Scientist, Sheffield Fertility Centre, Sheffield S7 1RA, UK;* [4]*CHILD, National Infertility Support Network, Bexhill on Sea, East Sussex TN40 1JA, UK; and* [5]*Portcullis Public Affairs, 26 Cadogan Square, London SW1X 0JP, UK*

Introduction

Reproductive health needs of the population

The importance attached to fertility and reproductive function has been a recurrent feature of societies throughout history. The United Nations (1948) has long respected the need of individuals to reproduce, declaring that "Men and women of full age, without any limitation due to race, nationality or religion, have the right to marry and to found a family".

At present, the single most important factor in National Health Service (NHS) funding for infertility treatment is geographical location. College of Health surveys (Wiles and Oddos, 1996) on the funding and provision of infertility services in the UK show that almost one quarter of health commissioners do not fund any of the modern assisted conception techniques, such as *in vitro* fertilization. Although government has encouraged the participation of patients in decisions within the health service, fewer than half the NHS trusts responding to the most recent surveys report consulting the public before agreeing their policy on the purchase of infertility services.

Funding for Tertiary Care of fertility problems in the UK varies widely. Some service commissioners in England refuse to fund any assisted conception techniques yet are willing to provide unlimited amounts of money for tubal surgery, as this falls within part of a general gynaecological surgery budget. Other service commissioners provide some funding for assisted conception, but provision varies widely. The obvious danger is that patients may be offered that which is available rather than treatments that may be more appropriate and cost-effective, but are not available because of geographical location.

The emotional and financial impact of infertility on population morbidity was considered by a National Infertility Awareness Campaign (NIAC) survey in 1997 (Kerr *et al*., 1999). Those surveyed experienced tearfulness (97%); depression and isolation (94%); anger (84%); inadequacy (72%) and guilt or shame (62%). The most disturbing finding was that 1 in 20 respondents said they experienced suicidal feelings. The same survey showed that whereas 71% of couples felt they would benefit from counselling, only 12% had received any. None of these results was a surprise to those experiencing infertility or who work in the field. People unaffected do not always understand these feelings. The extent of the psychological morbidity is even greater than that described, as the survey was of patients who wished to be parents and there is additional morbidity among patients' parents, who want to be grandparents. The breadth of the psychological morbidity is greater than the 15% of all gynaecological referrals that are for infertility. The cost benefit of improved infertility services would be huge. GPs can play a vital role in this improvement, as the proposals laid out here will demonstrate. The 1997 NIAC survey found that 53% of respondents felt that their GP did not provide them with sufficient information. GPs are valuable resources for patients and could provide information, initial protocol-driven investigation and referral to properly resourced fertility clinics. However, as a GP may see only two or three infertile couples per year, most will not have the time to be on top of information provision for that level of exposure. Although GPs could provide initial workup, it may be that the low throughput in Primary Care demands that information also be available in the fertility clinics. Perhaps a referral proforma sheet could guide the initial investigation and provide basic written information.

According to the Government Statistical Services, there is a steadily increasing proportion of women in the UK who have never had a child (Office of Population, Censuses and Surveys, 1994). Among women who were born in 1948, 13% were childless at the age of 35; this proportion had almost doubled for women born 10 years later and this trend seems likely to continue (Department of Health, 2002). Approximately one seventh of couples are involuntarily childless, although the exact number depends inevitably on how the complaint is defined. Medical definitions of infertility tend to emphasize the immediate problem brought to the consultation, reflecting the typically short-term interaction of many doctors, and particularly specialists, with their patients. Therefore, most accepted definitions involve the number of months before the consultation during which couples have been trying to become pregnant. When the lifetime experience of a couple's attempt to raise a family is considered, a quite different picture emerges: studies from Oxford and Copenhagen reveal that at least a quarter of all couples experience unexpected delays in achieving their desired family size (Green and Vessey, 1990; Schmidt *et al*., 1995), although only a half may seek treatment. In recent years, there

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has been an increase in publicity about infertility and reproductive medicine technologies, which has gone some way to reduce both the stigma of infertility and the reluctance of couples to seek advice.

Infertility as a complaint brought to medical attention is also on the increase for several reasons. The first reason is a secular change in family planning such that, among married women, the mean age of mothers at first birth in the UK is now 29 years, as opposed to 25 years a decade ago (Department of Health, 2002). This change seems to be a feature of the demography of many countries in the developed world. Age is so crucial a determinant of fertility that the increasing age at which many women now choose to start their family means that fertility problems feature more in their lives than ever before. It is naturally galling for a woman who has pursued safe contraception conscientiously for many years to find that, when she does plan to start a family, fertility eludes her.

Although the infertility itself is a psychological blow to the couple, the suffering is magnified if they find that NHS eligibility criteria exclude them from treatment, particularly when it is known that other couples in their situation are being treated. This inequality questions the name of any service with ‘National’ in its title. The National Health Service currently rations infertility treatment and does so on non-clinical grounds. The figures presented above clearly demonstrate a need that is not being met by the NHS.

Administrative environment in healthcare

The notion of ‘Quality in Healthcare’ in the UK has been developing for several years. Evidence-based care and subspecialisation have been the principles, while audit and clinical governance have allowed outcome measurement and quality control. The National Institute for Clinical Excellence (NICE) –Commission for Health Improvement (CHI) axis has produced the mechanism for driving improvements in quality of care.

Among health care specialties none can demand more immediate attention than cancer care; however, none can have lower current provision than fertility. Government attention to cancer care has produced a framework that ensures appropriate referral both in relation to speed and direction. Management has been streamlined to achieve rapid access and transit through the diagnostic system, while providing for the holistic needs of the patient (for example, investigations, counselling and home care). Laboratories work within extensive quality control safeguards. Treatment is evidence-based by recognized sub-specialists or named lead clinicians. Where evidence is not available, access into current trials can be sought. It is clear that provision of service in this framework has improved the quality of patient care both for specific diseases and from the perspective of the patient. Reducing circuitous referral routes and limiting inappropriate surgical intervention have saved resources for redirection to more productive areas (for a more detailed analysis, see Templeton *et al*., 1998). Investment seems to have yielded greater value than expected.

Fertility care in the UK is at a stage of development that cancer care had reached 10 years ago. The ‘postcode’ variation leads, in some areas, directly to Fertility Centres, and in other areas to general gynaecologists, who may have no direct professional links into Tertiary Care. Holistic patient care (for example, clinic environment, access to counselling, adequate consultation time and multidisciplinary teams) cannot be achieved against a backdrop of under-funding and fragmentation between Secondary and Tertiary Care.

In 2000, the Secretary of State for Health announced that fertility care was to be reviewed by NICE. The first meeting of the NICE Review Committee took place in the summer of 2002 and their deliberations are expected to be complete by autumn 2003. This paper has been written by a working group set up by the British Fertility Society in 2000 and collates evidence already available about effectiveness and costing. It supports the facts currently being addressed by NICE and considers the issues beyond those, to suggest a framework for implementation. The paper is intended to be considered by NICE and to be taken as a potential foundation of a framework for fertility care in the UK. However, our intention is not to provide a set of guidelines or to review the entire literature on infertility. For practical guidance on the management of infertility the reader is referred to publications such as *The Management of Infertility in Primary, Secondary and Tertiary Care. Three Sets of Guidelines* (RCOG Press, 1998a,b, 2000), *Evidence-based Fertility Treatment* (Templeton e*t al*., 1998) and *Infertility in Practice* (Balen and Jacobs, 2003).

Progress in fertility care

The first treatment to be provided for infertile patients involved relatively crude surgery. Treatment has become more refined and, in some cases, evidence-based (Saravelos *et al*., 1995). Through the 1970s the establishment of microsurgical techniques for tubal reconstruction gave hope to those with tubal causes of infertility and introduced the concept of best practice and audit in the management of infertile patients (Hull and Fleming, 1995). The development of assisted reproductive techniques (ART) initially in the form of *in vitro* fertilization (IVF) marked a step change in our ability to help the childless (Edwards *et al*., 1980). Unfortunately, well-motivated patients rather than research grants largely funded the development of those first cycles, hence the service developed in the private sector. Historically, therefore, the NHS did not have a budget for assisted conception treatment.

The evolution of ovulation-induction agents has also been driven largely by commercial interests. The anti-oestrogen clomiphene citrate is used primarily in the management of anovulatory infertility. Gonadotrophin preparations, although used for unifollicular ovulation induction, play a greater role in assisted conception protocols. The production of the first human menopausal gonadotrophins, their subsequent purification and the development of recombinant gonadotrophins (for a review, see Hayden *et al*., 1999) has only been achieved thanks to investment by the pharmaceutical industry.

Through the early 1990s, resource management was introduced into the NHS. New services required the support of business plans, which formed the basis of the NHS development. Assisted conception evolved from innovation to basic treatment without being incorporated into NHS core funding. The internal market of the 1990s enabled individual consultants and specialists in different areas in the NHS to make the case for services they wished to provide for patients in their area.

Those areas in which there were consultants with a special interest and particular training in assisted conception made the case for local provision, with varying responses from local health authorities. As a result, the NHS had different provisions for assisted conception in different health authorities, illustrating one of the first examples of what has colloquially been termed a 'postcode access to service'. Where services were provided, the contracts and agreements by which that service was supplied varied extensively in patient criteria for treatment, contract types (number of cycles or number of live births) and number of cycles allowed for eligible couples.

Although IVF itself is now far from new as a method of treatment, ART includes procedures, such as intracytoplasmic sperm injection (ICSI), which have been developed in the last decade. Furthermore, technology is progressing rapidly and new advances sometimes enter clinical practice, after initial trials. Thorough investigation should continue of the safety and effects on children born as a result of, for example, ICSI, preimplantation genetic diagnosis, *in vitro* maturation of oocytes, blastocyst culture, ovarian cryopreservation, stem cell culture and cloning. Some follow-up is undertaken but it might be better if there was seamless provision between Tertiary and Secondary Care within an adequately funded NHS-based system. Reproductive medicine often makes headline news because of the controversial and ethically challenging nature of some of the new technologies (as indeed was the case when IVF itself was introduced).

Infertility, as a symptom, has many causes that can loosely be divided into failure to ovulate (treated mainly either by oral clomiphene citrate or injectable gonadotrophin preparations), failure of normal sperm output (usually treated by IVF or ICSI but sometimes requiring donor insemination), mechanical blockage in the female genital tract (requiring either surgery to the Fallopian tubes or IVF) or the male genital tract (requiring either microsurgery but, more often, surgical collection of spermatozoa and then IVF–ICSI). All of these therapies require specialist knowledge and multidisciplinary skills. Tubal surgery is a good example, as it has been performed inappropriately as a 'gynaecological surgical procedure' under a normal gynaecology budget, often by generalists rather than by subspecialists with access to appropriate equipment. Thus, many women have had sub-optimal surgery for two reasons. First, they may have had conventional rather than microsurgery; second, they may have had surgery when assisted conception was indicated because funding for assisted conception was not available.

Current evidence

Primary care

The Royal College of Obstetricians and Gynaecologists (RCOG) has laid out primary health care guidelines (RCOG, 1998b) on the initial management of infertile couples. Adherence to these guidelines before referral into Secondary Care varies. Data presented in the *Evidence and Equity Document* by the Expert Advisory Group on Infertility Services in Scotland (EAGISS, 1999) indicated that, at the time of referral for Secondary Care, little more than 50% of female partners had had assessment of ovulation by measurement of plasma progesterone. Moreover, only 10–15% of patients had had rubella immunity status established. Only 35–45% of the male partners had had a semen analysis performed before referral. EAGISS also identified a number of unnecessary investigations that had been performed in level one care, such as thyroid function testing in regularly menstruating women (19%). It is clear that if the entry criteria into hospital-based infertility care were tightened to make appropriate investigation in Primary Care a prerequisite to referral, a significant number of hospital consultations could be avoided, resulting in enhanced efficiency. The cost savings could be distributed further along the process of investigation and treatment, reducing waiting times and unnecessary investigation as well as contributing to the funding of treatment currently unavailable. This is self-evident quality improvement.

Secondary care

The *RCOG Secondary Care Guidelines* (RCOG, 1998a) recommend that fertility patients should be seen in a "dedicated infertility clinic staffed by an appropriately trained multiprofessional team with facilities for investigating and managing problems in both partners". That team should include access to infertility counsellors. The Secondary Care provision of treatment may include treatment of anovulation, in which case the use of anti-oestrogen preparations such as clomiphene "should only be performed in circumstances which allow access to ovarian ultrasound monitoring". Furthermore, ovulation induction with gonadotrophins requires particular expertise and adherence to firm guidelines (Balen, 1997, 1998). If surgery is proposed for tubal infertility, it is well established that "when distal tubal surgery is performed a microsurgical approach using magnification should be used". With regard to endometriosis-associated infertility, the disease "should be classified using the revised American Fertility Society system" and "surgical ablation of minimal and mild endometriosis" appears to be the treatment of choice and should be available through the dedicated clinics, preferably at the time of the diagnostic laparoscopy (Marcoux *et al*., 1997).

As with Primary Care, efficiency can be enhanced in Secondary Care using evidence-based care pathways. The improvement yield may be direct (for example, the cost savings by microsurgeons only selecting appropriate cases for surgery) or indirect (for example, appropriate monitoring of ovulation, facilitating reduction of the neonatal and social costs of multiple pregnancies) (Levene *et al*., 1992). Finally, there is an improvement in quality of care that will be evident to the patient who can be given evidence-based advice, as illustrated by the treatment of patients with endometriosis with endoscopic surgical ablation rather than months of expensive gonadotrophin releasing hormone analogue treatment, which is of significantly less benefit to fertility (Hughes *et al*., 1999).

Patients in the Secondary Care environment should not have routes of care limited by that environment; referral into Tertiary Care should be seamless. Patients attending a Secondary Care unit which itself does not undertake Tertiary Care should not be cared for in any way less effectively than if they were having that Secondary Care in larger Tertiary Care units. It is important to have a network of Secondary Care providers who are named gatekeepers into Tertiary Care, with properly funded,

dedicated time and space on their timetable for this function. A multidisciplinary team is required from the moment of referral from Primary Care.

Tertiary care

The RCOG has provided evidence-based guidelines for Tertiary Care (RCOG, 2000). However, practice is highly regulated by the Human Fertilisation and Embryology Authority (HFEA), whose jurisdiction covers most of what is regarded as Tertiary Care.

The evidence-based RCOG guidelines need to be prioritized when planning service development. This involves a balance between cost and effectiveness. For example, unstimulated intrauterine insemination (IUI) as a treatment for mild male factor infertility has been quoted as being 'cost-effective' in certain situations. However, the actual effectiveness is so variable that its use may not be justified despite its relatively low cost. It should certainly be an option in units that can demonstrate its effectiveness. However, the situation in which IUI is used as a treatment merely because more suitable treatments are not available should be avoided by the use of appropriately directed funding. This is the sort of area in which evidence-based medicine needs to be used in conjunction with common-sense service delivery considerations.

However, it is reasonable to expect that the combination of gonadotrophins to induce superovulation (with the release of two or three oocytes) with insemination of a prepared sample of spermatozoa into the uterine cavity should boost fertility in cases of unexplained infertility, although there are contrasting studies in the literature. Melis *et al*. (1995) reported a large prospective, randomized study comparing gonadotrophin therapy and timed intercourse with gonadotrophin therapy and IUI. Two hundred couples with at least 3 years' unexplained infertility received superovulation with FSH to produce at least two follicles. There was no significant difference in the outcome of the two groups, but a cumulative conception rate of approximately 43% after three cycles and a multiple pregnancy rate of 10%. A meta-analysis by Hughes *et al*. (1997) indicated that superovulation with IUI and stimulation with FSH alone each increase fecundity twofold, whereas combining these treatments results in a fivefold increase.

When planning reform, it should be possible to prioritize the changes. Weighting should be given to the quality of evidence. For this reason, the current primary, secondary and tertiary RCOG Guidelines have been summarized to highlight the Grade A Evidence, which should be considered as top priority for reform of the system (Box 1). Evidence categorized as grade B or C, although less robust, should not be ignored. At present, NICE is reviewing guidelines and may well provide updates on the levels of evidence in the foreseeable future. However, the concept of evidence weighting is clearly demonstrated.

Cost

The other parameter of prioritization is cost. Clear cost–benefit margins must enhance the prioritization of particular investigations or treatments. The York Health Economics Consortium (1999) reported on the *Evaluation of the Relative Cost-effectiveness of Treatments of Subfertility*. This was more than merely a formula for a protocol, as the consortium included other considerations. An analysis of the work was provided by Philips *et al*. (2000), who looked at various treatment modalities in the different diagnostic groups of subfertility. There was a high correlation between the cost-effectiveness analyses and the RCOG treatment guidelines, although, as the outcome measure was clinical pregnancy, no account was taken of the cost of complications such as ectopic pregnancy or the additional costs of the care associated with multiple pregnancies. Therefore, the conclusions of Phillips *et al.* (2000) are subject to variation in relation to factors such as the diversity of costs of assisted conception, number of embryos replaced and number of cycles funded. However, the conclusions could become the foundation upon which recommendations for NHS provision might be based. Phillips *et al*. (2000) reported that:

- IVF is the most cost-effective treatment of infertility due to severe tubal factor and severe endometriosis.
- Tubal disease that is mild or moderate might be considered for surgical treatment.
- Microsurgery for proximal tubal disease is preferable to conventional surgery. The endoscopic approach is of benefit when undertaking adhesiolysis.
- There may be some benefit in removing hydrosalpinges prior to IVF treatment (Strandell *et al*., 1999).
- Endometriosis that is mild or moderate is more cost-effectively treated surgically.

Not all of the data on cost-effectiveness are as clear-cut. They indicate that bromocriptine should be the first-line treatment for hyperprolactinaemia, yet cabergoline is better tolerated and for this reason is more widely prescribed. Clomiphene is proposed as the first-line treatment for other causes for anovulation. The suggested second-line treatment for patients with polycystic ovary syndrome (PCOS) is endoscopic ovarian drilling but, for patients who do not have PCOS, it is the use of pulsatile GnRH. Gonadotrophin treatment is a third option for each condition. These statements, while perhaps representing cost-effective treatment, are not based on sound evidence (Balen, 1998). Indeed, there are no adequately powered prospective randomized trials on either first-, second- or third-line therapy for anovulatory PCOS.

For male factor infertility, patients with very mild abnormalities may achieve pregnancies with no treatment, whereas those with moderate abnormalities have been shown to benefit from stimulated IUI, which, because of the cost differential, has been shown to be more cost-effective than IVF or ICSI. For severe male factor problems, there is no doubt about the cost-effectiveness of donor spermatozoa. However, patients have a natural desire for their own genetic offspring. ICSI and, if necessary, surgical sperm retrieval may result in greater expense per pregnancy than use of donor spermatozoa but there is a difference in the 'quality' of the outcome of the two treatment modalities perceived by the patients. Different patients may have differing perceptions, so both donor sperm and ICSI–sperm retrieval should be available for discussion between the patient and their clinician. Finally, the role of stimulated IUI in the treatment of unexplained infertility is still being debated,

despite evidence of its efficacy (Hughes, 1997). The return in pregnancies is relatively low, but so is the cost. It is arguable that one cycle of IVF might reasonably be undertaken in the unexplained infertility group as it provides both the treatment and investigation of sperm–oocyte function (that is, fertilization). In the presence of good quality embryos but the absence of an established pregnancy, subsequent cycles of IUI might be regarded as a reasonable course of management.

In conclusion, the main indications for IUI appear to be mild male factor and unexplained infertility after one cycle of IVF has resulted in the generation of good quality embryos. Indications for IVF specifically include failed tubal surgery, severe tubal disease and endometriosis, and severe male factor in addition to unexplained infertility. There is a role for IUI, but it is somewhat limited. Funding for these services if directed appropriately can be made more efficient. This efficiency, in addition to the savings mentioned above, may, at least in part, offset costs of fertility service development as a national Fertility Plan.

A further consideration is that, at present, success rates from assisted conception units vary among units and within a single unit from year to year, and between patients by age of female partner and cause of infertility. Costs per cycle of assisted conception, if funded extensively throughout the UK, might be expected to drop as a result of the increased throughput. Moreover, there are small year-on-year increases in success rates albeit small. Therefore, there is likely to be a trend towards improved cost-effectiveness over time. The threshold for surgery for tubal disease may increase as the increase in success rates for ART exceed those for microsurgery. This effect will be magnified by the reduction in the number of gynaecologists interested and skilled in microsurgery and the fact that IVF can be delivered in an outpatient setting.

These developments and the fact that most of the RCOG Guidelines are not based on Grade A Evidence demand that some flexibility in practice be available as the evidence develops.

There is considerable debate on how many cycles of assisted conception should be funded. In global terms, there are huge variations in the numbers of cycles permitted within different government and insurance programmes. For example, in South Australia, there has been a recent extension of the permitted number of cycles from five to unlimited, possibly as a result of the insurance-based system in that country. However, it reflects a confidence that the decision-making process between doctor and patient will not lead to unnecessary treatment.

EAGISS (1999) recommends funding a basic three cycles, counted as embryo transfers. As a group, we did not feel there should be fewer. However, there may be an opportunity to develop a public–private partnership for subsequent cycles. In general, the private insurance market in the UK provides for those services that the NHS does not do well (for example, that have long waiting lists) and not those services the NHS does not cover at all. Therefore, IVF, which is not funded at a national level within the NHS, is not covered by any private insurance. If the NHS were to provide, say, 100% funding of the first three cycles, the subsequent cycle could be, say, 75% funded and the following cycle 50% funded. This would create a buffer zone within which there may be the possibility to establish a private insurance market, in effect, a public–private partnership. Uninsured patients would not then reach a sudden void of provision, while it would allow insurance companies to market a product that covers the difference for these subsequent, partially funded cycles. Both the NHS and the insurance companies could then rest assured that there was a cap to their spending. Moreover, the number of cycles funded is not a simple multiplication of the cost, as the number of patients returning for repeated cycles diminishes sequentially because of pregnancies in each of the successive attempts.

Although not included in the RCOG Guidelines, reproductive services for those undergoing treatment for malignancy should be included in future planned provision and funding. A separate document should consider this major subject. Moreover, the Government should consider implementing the recommendations of the *McLean Review* (1997) to enable the effective consent provisions in the *Human Fertilisation and Embryology Act 1990* to be waived in respect of children and adults who are unable, because of incapacity, to give effective consent to storage of their mature gametes or tissue containing mature gametes. There should be a comprehensive nationwide service covering the initial freezing and long-term storage of mature spermatozoa for men and competent boys facing sterilizing therapy and the development of appropriate fertility preserving services for others facing sterilizing therapies, including girls, women and prepubertal boys.

Structural framework for provision

It is important to have the infrastructure to administer fertility services otherwise the new service will appear disorganized. NHS services require medical and paramedical support as well as adequately equipped premises. Although much of this provision is in place, consistent quality standards should be set. The role of the HFEA could be extended, with appropriate funding.

The framework for the provision of fertility care should be seamless, from GP to sub-specialist. Care and funding are interdependent and it may be preferable not to separate primary, secondary and tertiary provision. The framework that is proving so successful in providing for cancer patients might offer a template for subfertility services. Rather than Secondary and Tertiary Care we should consider 'Fertility Units' and 'Fertility Centres'. GPs will provide certain data on a *proforma* as a prerequisite for patient appointments in a local fertility unit, thereby ensuring that the preliminary workup has been done before attendance at the fertility unit. Fertility centres will provide what is described in the RCOG guidelines as Tertiary Care. Much Secondary Care will also be provided here but designated Fertility Units will encourage some care to be undertaken at hospitals remote from the Fertility Centre. Lead clinicians, who might not undertake tertiary work themselves, could run these Fertility Units and submit audit reports to ensure consistent quality of care and adherence to guidelines. Fertility Centres, since they would be undertaking Tertiary Care, would continue to be subject to HFEA audit returns. Laboratory practice should be subject to the same quality control as in cytology laboratories.

Unnecessary delays adversely affect treatment success rates in fertility care. The fact that fertility is of less urgent status than cancer in terms of waiting lists ought not to make it less important. Delays in investigation and treatment, and

Box 1. Grade A Evidence* summarized from the current Primary, Secondary and Tertiary Royal College of Obstetricians and Gynaecologists guidelines

Primary Care

1. Local protocols based on these guidelines should be agreed for the general practice management and referral of infertile couples.
2. GPs should advise women presenting with infertility to take 0.4 mg folic acid per day as a daily supplement while they are trying to conceive and during the first 12 weeks of a pregnancy in order to prevent neural tube defects. The dose should be increased to 4 mg per day in women who have previously had an infant with a neural tube defect or who have epilepsy and are taking medication.
3. The body mass index (BMI) of the female partner should be calculated as part of the primary care management of infertility. A supervised weight loss programme is advised for any woman with a BMI > 30, whether or not they are ovulatory.

Secondary Care

1. Intrauterine insemination with or without ovarian stimulation is an effective treatment if the man has abnormalities of semen quality, but it has to be remembered that pregnancy rates, even after treatment, remain very low.
2. Infection of the male genital tract should be treated if present, but there is no evidence that this will improve fertility.
3. Anti-oestrogens, androgens, bromocriptine and kinin-enhancing drugs have not been shown to be effective in the treatment of men with abnormalities of semen quality.
4. There is evidence that semen quality and pregnancy rates may improve in oligozoospermic men after treatment of a clinically apparent varicocele (A). Treatment of a varicocele in infertile men with normozoospermia has not been shown to be beneficial.
5. Clomiphene is an effective treatment for anovulation in appropriately selected women (A). (Up to 12 cycles of treatment should be considered (B).)
6. FSH and human menopausal gonadotrophin (hMG) are both effective for ovulation induction in women with clomiphene-resistant polycystic ovarian syndrome (PCOS).
7. There is no advantage in routinely using gonadotrophin-releasing hormone analogues in conjunction with gonadotrophins for ovulation induction in women with clomiphene-resistant PCOS as there is no increase in the pregnancy rate (A). (Furthermore, their use may be associated with an increased risk of ovarian hyperstimulation (C).)
8. Laparoscopic ovarian drilling with either diathermy or laser is an effective treatment for anovulation in women with clomiphene-resistant PCOS (A). (However, more research is needed into the sequelae of causing ovarian damage in this way (C).)
9. Dopamine agonists are effective treatment for women with anovulation due to hyperprolactinaemia.
10. Surgical ablation of minimal and mild endometriosis improves fertility in subfertile women.
11. Medical treatment of minimal and mild endometriosis does not enhance fertility in subfertile women.
12. Ovarian stimulation with intrauterine insemination (IUI) is more effective than either no treatment or IUI alone in subfertile women with minimal or mild endometriosis.
13. There is no evidence that medical treatment of moderate and severe endometriosis, either alone or as an adjunct to surgery, improves fertility.
14. Ovarian stimulation with intrauterine insemination is an effective treatment for couples with unexplained infertility.
15. Gamete intra-Fallopian transfer (GIFT) is an effective treatment for couples with unexplained infertility (A). (However, IVF may be preferred because of the additional diagnostic information it provides and because it avoids laparoscopy and, possibly, general anaesthesia (C).)
16. Current evidence indicates that the treatment of unexplained infertility with clomiphene will result in little or no benefit (A). (Therefore, this treatment should be used only in the context of a large randomized controlled trial (C).)
17. Danazol is not effective in treating couples with unexplained infertility.
18. Bromocriptine is not effective in treating couples with unexplained infertility.

Box 1. continued

Tertiary Care

1. In IVF treatment, the use of GnRH agonists in addition to gonadotrophin stimulation results in higher pregnancy rates than the use of gonadotrophins alone. Therefore, the routine use of GnRH agonists in IVF stimulation protocols is recommended.
2. There is a small but significant increase in pregnancy rates after the use of high-purity gonadotrophin preparations derived from urine when compared with human menopausal gonadotrophin preparations.
3. Recombinant FSH produces significantly more oocytes in an IVF cycle than do high-purity gonadotrophin preparations derived from urine; however, pregnancy rates in fresh embryo replacement cycles are similar.
4. If fresh and frozen embryo replacements are considered, the use of recombinant FSH produces a higher pregnancy rate compared with high-purity gonadotrophin preparations derived from urine.
5. Variations in embryo transfer technique can affect outcome. Placement of embryos in the mid-cavity of the uterus preceded by a trial with a dummy catheter is most likely to result in a pregnancy. A tubal embryo transfer followed by bed rest have not been shown to improve outcome.
6. In IVF cycles in which GnRH agonists are used for pituitary downregulation, luteal phase support results in higher pregnancy rates. The choice of luteal phase support is between hCG and progesterone, and whereas hCG may result in higher pregnancy rates, there is an increased likelihood of ovarian hyperstimulation syndrome, and for this reason the routine use of hCG is not recommended.
7. Transport IVF–ICSI results in fertilization, implantation and pregnancy rates that are similar to those achieved with conventional one-centre treatment.
8. If the anticipated pregnancy rate for intracervical insemination is $< 6\%$ per cycle, intrauterine insemination with or without ovarian stimulation should be considered.
9. Assisted hatching has not yet been shown to be an effective treatment.

*Grade A evidence should be considered as the top priority for reform of the system. Evidence categorized as grade B or C, although less robust, should not be ignored.

inappropriate detours through less effective treatment routes affect outcomes significantly. Time-related deterioration in live birth rates wastes resources that could be better directed. The fertility plan outlined above would address this and improve care, and make funding equitable and efficient.

Eligibility criteria for Tertiary Care

NHS-funded assisted conception should be available ideally to all who require it on the basis of medical decision-making in consultation and agreement with the patient. However, cash limitation on provision has prompted health commissioners in the UK to consider restrictive criteria as a form of rationing. There are situations in which the restrictions involve the exclusion of patient groups for whom treatment is more likely to succeed (for example, those with proven previous fertility). Selection criteria around the country include:

- Age of woman
- Age of man
- Number of children from previous relationship
- Duration of relationship
- Length of residence in funding catchment area
- Number of previous cycles
- Smoking habit
- Body weight

Allocation of services on criteria such as the above amounts to rationing and is to be deplored. Removal of restrictions need not lead to large increases in demand as recent changes in Australian service provisions have shown. There needs to be a balance between clinical advice about effective treatment options and patient education about realistic pregnancy rates from different treatments. Therefore, restriction becomes a cost-effective decision between professional and patient in the consulting room. State rationing is not necessary. Appropriately counselled patients and responsible clinicians reach appropriate clinical decisions without the need for government rules.

Key proposals: the Fertility Plan

1. Introduce national funding of primary, secondary and tertiary levels of care for the infertile couple, eliminating postcode inconsistencies
   a. Base funding on RCOG guidelines for indications with consideration of the effectiveness of treatments as well as their costs
   b. Fund a service for young patients undergoing treatment for malignancy
2. Improve patients' perspective of their care
   a. Establish a role for Primary Care in the initial investigation which fulfils entry criteria into the fertility service
   b. Provide the fertility service within a Fertility Centre–Fertility Unit structure, thereby minimizing repeat investigation and consultation, producing a seamless care pathway
3. Improve the quality of care through a framework for service, in which:
   a. Fertility Units and Centres partake actively in audit
   b. Laboratory support, particularly for andrology, is subject to the same quality standards as are applied to cervical cytology
   c. The system of Fertility Units and Centres ensures that patients being referred from Primary Care are entering a system within the fertility service with access to all levels of care

Time course

It is important that infertility treatments and their indications are considered by NICE as quickly as possible. Deliberations are expected to continue throughout 2003. Once the nature of the NHS commitment is established, the size of the service can be planned and Fertility Centres specified, preferably as close to patient's homes as possible, thereby avoiding long journeys during treatment cycles. A working party should set up facility networks linking future Fertility Centres and Units, as well as initiating negotiations with the private sector.

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