Rachel's ladders or how societal situation determines reproductive therapy

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Introduction

The evolving social justice basis for health care questions the historical right of those whose feet firm higher societal ladder rungs to receive better health care than those on lower rungs. In some societies, mainly European, this social justice foundation now affords prescription of therapy specific to each patient's medical problem, regardless of the socio-economic ladder rung on which the patient's foot rests. But in most 'developed' countries, health care personnel must still consider each patient's societal ladder location in therapeutic decision-making. In so doing we inadvertently become complicit to the construction of therapy ladders, whose cost-dependent rather than aetiology-dependent rungs may commit our patients to less than 'good' therapy from 'good' physicians.

Reproductive medicine, due to the non-life threatening nature of our patients' problems, is particularly prone to ransom by government and third party insurers, who inflict inequity in the name of health care rationalization and profit maximization respectively. The global trend towards decreased government funding of health care abuts on the continued increase in cost of therapy (Daya et al., 1995). As the fiscal quests of health care 'providers' become increasingly demanding, our patients become increasingly vulnerable to suboptimal care, and we increasingly become considered as cosmetic surgeons, prescribers of elective therapy.

The reproductive therapy ladders in Figure 1 are aetiology-specific. All women on a particular ladder may be considered to have identical infertility problems; the rung on which a woman's foot rests purely reflects her socio-economic status rather than her specific infertility problem. The rung assignment by proclaiming her therapy, determines her chance of pregnancy, morbidity, and complication risk. The first ladder in Figure 1 holds women with identically damaged Fallopian tubes (grossly dilated with no fimbria), the second holds women with identically poor quality and quantity of oocytes, and the third holds women whose partners have identically severe sperm problems. The ladders are constructed with therapies of high cost, high effectiveness (and usually low morbidity) as high rungs, and therapies of low cost, low effectiveness (and usually higher morbidity) as low rungs (with the exception of donor insemination on the sperm problem ladder discussed below).

Therapy ladder for damaged Fallopian tubes

Let us first consider how the rung on the reproductive therapy ladder holding a woman with severely damaged Fallopian tubes determines pregnancy potential, morbidity and risk of therapy-induced complication (Figure 1A). Up to 15 years ago, the only therapy available for a woman with markedly dilated tubes and agglutinated fimbria was tuboplasty. For a <5% chance of a child (Fayez, 1983; Toback, 1992), women endured the morbidity of general anaesthesia and laparotomy. Even when surgery on severely-damaged Fallopian tubes resulted in pregnancy, 25–100% (Fayez, 1983; Benadiva et al., 1995) of the pregnancies dangerously occurred in the Fallopian tube, sentencing the woman again to further morbidity and risk for pregnancy removal. In 1996 a woman perched on the top rung of the tubal disease ladder (Figure 1A) may choose in-vitro fertilization (IVF) to bypass her damaged Fallopian tubes and optimize fertilization and implantation by gamete micro-manipulation techniques such as intracytoplasmic sperm injection (ICSI) (Van Steirteghem, 1993, 1995; De Jonge and Pierce, 1995) or hatching (Katayama, 1994). The rung beneath, of standard IVF, affords a woman with tubal disease up to a 25% chance of pregnancy per cycle (Oehninger et al., 1989). Although the morbidity of oocyte retrieval and the menotrophin-induced risks of ovarian hyperstimulation syndrome (OHSS) (Schenker and Ezra, 1994) and possibly ovarian carcinoma (Lopes et al., 1993; Shoham, 1994) must be stressed, the financially-fortunate women on these top rungs have a much higher chance of pregnancy than women on lower rungs. They also avoid general anaesthesia and laparotomy and dramatically reduce the chance that their pregnancy will occur in a Fallopian tube (Daniel, 1995).

A woman situated further down the tubal disease ladder does not possess the financial resources for a standard IVF cycle but may accept a 'discount' IVF cycle if she will 'share' her eggs with a wealthy couple. Although a woman on this rung compared to a woman on the tuboplasty rung below may anticipate less morbidity and complication risk, as well as a higher pregnancy rate, she suffers a lower per cycle pregnancy rate than the woman on the rung above whose financial status precludes giving up eggs and the potential embryos they represent (with cryopreservation and later uterine transfer). An increased morbidity and complication risk
A. Damaged Fallopian tubes

- IVF + micromanipulation
- IVF
- IVF-oocyte sharing
- Tuboplasty
- Ovarian stimulation with IUI

B. Oocyte depletion

- Purchase oocytes
- ICSI
- IVF
- IVF-oocyte sharing
- Ovarian stimulation with IUI

C. Severe sperm problems

- ICSI
- ICSI + oocyte sharing
- IVF
- IVF-oocyte sharing
- Ovarian stimulation with IUI

* Exception to highest chance of pregnancy with highest cost

Figure 1. Description of reproductive therapy ladders for A: severely damaged Fallopian tubes; B: oocyte depletion and C: severe sperm problems. IVF = in-vitro fertilization; IUI = intrauterine insemination; ICSI = intracytoplasmic sperm injection; DI = donor insemination.

(Schenker and Ezra, 1994) may also be anticipated as more cycles of menotrophin stimulation and oocyte retrieval may be required to achieve the same chance of pregnancy.

The therapy ladder for severe tubal disease, ovarian stimulation with menotrophins and intrauterine insemination (IUI) is inadvertently encouraged by drug plans or social assistance programmes that pay for menotrophins in combination with a health care system that does not support IVF. The chance of achieving a child on this rung is remote and an unfortunate option considering the potential risk of menotrophin therapy (Schenker and Ezra, 1994). It seems archaic that in many ‘developed’ countries today, women with damaged Fallopian tubes whose feet adhere to low rungs of the socioeconomic ladder (and thus reproductive therapy ladders) are required to ‘share’ eggs, suffer tuboplasty, or accept totally ineffective therapy.

Therapy ladder for oocyte problems

It is poorly understood why some women continue to produce fertilizable oocytes in their mid-40s and beyond, while other women have few functioning oocytes remaining much earlier in life. Recent reports indicate that even women with regular menstrual cycles may possess few remaining fertilizable oocytes if a cycle day 3 serum follicle stimulating hormone (FSH) determination is >20 mIU/ml (Martin et al., 1995). The trend to pregnancy delay in the last two decades (Baird, 1993) has perhaps increased the frequency of this aetiology.

The therapy ladder holding a woman with oocyte depletion or suboptimal function (Figure 1B) is again quite steep. The highest rung supports couples who have sufficient financial resources to purchase oocytes, either from a woman with tubal disease on a low ladder rung, who must sell her eggs to afford an IVF cycle (Figure 1A), or from a fertile woman whose financial misfortune impels her to undergo IVF and sell eggs as a source of income. The couple receiving this high-rung therapy will probably have >25% chance of achieving a child in each ‘donation’ cycle (Sauer et al., 1994). Another high-rung option is IVF with micro-assisted hatching (Katayama, 1994), or ICSI (Van Steirteghem et al., 1993) to optimize the fertilization of the few oocytes obtainable through menotrophin stimulation of women with oocyte problems and assist implantation of any embryos that might indeed develop.

The lower rungs of this therapy ladder (Figure 1B) hold women who cannot afford therapy other than ovarian stimulation with IUI and who choose to receive large quantities of menotrophin to cause any remaining oocytes to surface, even though the chance of pregnancy is <5% if even one serum FSH determination is >20 (Martin et al., 1995). As menotrophin stimulation of the ovary may be associated with ovarian carcinoma (Lopes et al., 1993; Shoham, 1994), this rung may be problematic from both a medical and purely moral perspective (Nisker, 1995).

Therapy ladder for severe sperm problems

Therapies offered for a severe sperm problem appear in the ladder illustrated in Figure 1C. Although ICSI (Van Steirteghem, 1993) is the highest rung (37% pregnancy rate per transfer) and eagerly received by couples who can afford the $6000-10,000 cost, the lower rung of donor insemination (DI) is the most effective and safest therapy for sperm problems. The lower rung location is in keeping with its lower desirability among couples who can afford ICSI-generated.
Table I. Pregnancy rates in cases with severe sperm problems: University Hospital, Ontario, Canada, 1992–1994

<table>
<thead>
<tr>
<th>Programme</th>
<th>Cycles</th>
<th>Embryo transfer (%)</th>
<th>Pregnancies</th>
<th>Pregnancy/cycle (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF</td>
<td>49</td>
<td>37.5</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>PZD or SUZI</td>
<td>130</td>
<td>50</td>
<td>10</td>
<td>7.7</td>
</tr>
<tr>
<td>ICSI</td>
<td>226</td>
<td>90.3</td>
<td>46</td>
<td>19.5</td>
</tr>
</tbody>
</table>

IVF = in-vitro fertilization; PZD = partial zona dissection; SUZI = subzonal insemination; ICSI = intracytoplasmic sperm injection.

*78% were too severe to qualify for standard IVF, PZD or SUZI.

Genetically-related children. Data from our unit (Table I) suggests that the chance of achieving pregnancy with therapies on rungs other than DI or ICSI is extremely low. The fact that ovarian stimulation with IUI and standard IVF continue to be accepted by women as treatment for their partners’ severe sperm problems is testimony to the desperation of infertile women. An evidence-based approach to therapy for severe sperm problems would restrict the therapeutic options to the ladder rungs of DI and ICSI (in an experimental context only).

The morality of allowing a woman to suffer multiple cycles of gonadotrophin stimulation and the potential risk of ovarian cancer and severe OHSS (as well as oocyte retrieval for IVF) for a small chance of pregnancy will be discussed below under morality of therapy restriction.

Geographic location of ladders

Geographic location determines the existence and slope of reproductive therapy ladders. A woman geographically situated in a country that does not sponsor funding for reproductive therapy, such as the USA or Canada, is afforded lower rung therapy than a woman whose infertility aetiology is identical but who lives in Australia (where six IVF cycles are government sponsored), in France (where four cycles are funded), or in Israel (where IVF is funded until one child is born). Indeed in Australia, France and Israel, a woman on a low socio-economic ladder rung receives higher reproductive therapy rung treatment than women of middle income in the USA or Canada.

Although the country in which the ladder stands, by ‘virtue’ of federal government sponsorship, may be the major geographical determinant of ladder position, often the province, state, or District Health Authority (DHA) within that country determines the ladder’s angle of inclination and even the construction of the ladder itself. For example in the UK, 30% of DHA support IVF funding (Wiles and Wilson, 1994). If the woman lives in Scotland where all DHAs afford full funding of reproductive therapy, she may choose to receive much higher ladder rung therapy than a woman in Northern Ireland where none of the DHAs include IVF in their list of provided services (Wiles and Wilson, 1994). In Canada, where only the province of Ontario includes IVF as a funded service (restricted to bilateral blocked Fallopian tubes since April 1, 1994), and in the USA, where only the state of Massachusetts funds IVF, region-specific ladder rung assignment again determines the therapy option, the chance of having a baby, treatment morbidity, and risk.

The extreme cost of infertility medication also contributes to the influence of geographical location on the infertility treatment ladders’ slopes. In UK, family physicians and DHAs vary in their inclusion of medication directed towards treatment of infertility in their list of insured medications. In Canada and the USA, some private drug plans will cover menotrophins for a specific number of cycles or pre-set dollar determination, but most couples have no drug plan. Although occasional drug plan provision of medication allows some couples to receive the highest rung therapy possible, for others, non-availability of medication impels acceptance of bottom rung therapies for aetiology for which the therapy was not designed (such as ovarian stimulation/IUI for damaged tubes or severe sperm problems).

Government funding does not always prevent therapy ladders

Socio-economic ladders create therapy ladders not only because of funding restriction but also because women on the lower socio-economic rungs are less likely to avail themselves of funded services. In France, where the federal universality of health care took over reproductive therapy and chopped down reproductive therapy ladders, women on lower socio-economic ladder rungs are still less likely to receive high rung fertility therapy (de Mouzon et al., 1993). It is possible that suboptimal knowledge of options, financial considerations related to travel or time off work, lack of an environment suitable for raising children or the costs of raising children, remain obstacles in discouraging many French women from choosing high-rung reproductive therapies. There are no data to show whether these women undergo tuboplasty or other low-rung therapies, as would be the case for women on a similar socio-economic rung in countries where funding restriction has constructed reproductive therapy ladders. Another social factor restricting access to the top therapy ladder rungs may be lifestyle (Brewaeys et al., 1995). Sexual orientation and marital status have long impeded access to reproductive therapy (Sherwin, 1992; Shanner, 1995). In France, a couple unit must exist for at least 2 years before funding is available (Balter, 1994). Thus, even in the presence of well-funded, social justice-based health care systems, infertility treatment ladders may still exist.

Morality of ladders and self-perpetuation

Based on social justice precepts such as Kant’s first categorical imperative ‘that one should only act according to principles which can be applied universally’ (Kant, 1983), many consider health care to be moral only when equally available to all members of society (Nisker, 1995). Sam Gorovitz’ claim that ‘a state’s morality may be judged by how it cares for its weakest constituent’ (Gorovitz, 1994), suggests a moral state must afford equal health care to citizens on all socio-economic ladder rungs.

Shenfield and Steele (1995) question the presence of justice when IVF patients ‘share’ or ‘donate’ (which they call ‘selling’)
oocytes to receive IVF, citing Kant's second categorical imperative: 'treat all humanity always at the same time as an end and never merely as a means' (Kant, 1964). Shenfield and Steele (1995) propose that 'trading and buying persons (as in slavery) or his/her products (i.e. organs or gametes) entail treating the person or his/her products as mere means and is thus demeaning and an affront to the respect due to human beings'. As only a woman on a low socio-economic rung would ever consider 'sharing' or 'selling' her eggs (and accepting the lower pregnancy rate), distributive justice is ignored. In countries where justice includes equal access to infertility treatment, women have no need to 'sell' their eggs and this ladder rung does not exist (Nisker, 1995). Indeed all ladder rungs giving up oocytes were absent in Canada until the above-mentioned date of April 1, 1994, delisting IVF, but now 'voluntary sharing' of oocytes is the only way many Canadian women can receive IVF.

The defence most often put forward for the therapeutic discrepancy inherent in ladders is respect for personal autonomy (Macklin, 1987; Engelhardt, 1996). A purely autonomic perspective allows society, through its elected policy-makers, the right to decide against universal health care (or decide for universal health care but exclude reproductive therapy as an insured service). Such a perspective allows couples on a high socio-economic ladder the right to use their wealth to purchase any high-rung therapy technically possible, and couples on a low societal rung the right to choose whatever therapy they can afford, even if the therapy is largely ineffective. Autonomy also allows physicians and scientists the right to profit (academically, financially, or spiritually) from delivering therapy on any ladder rung, as well as the right to refuse any therapy they feel inconsistent with the best interests of their patient or themselves. The best interest of embryos and future children adds a complexity that must be explored thoroughly, but is beyond the scope of this paper (Benagiano and Rowe, 1995; Brewaey et al., 1995; De Jonge and Pierce, 1995; Van Steirteghem, 1995).

Previously, I have (Nisker, 1995) brought forward Howard Brody's (1985) argument that when a therapy of minimal chance of positive outcome is offered, choice is implied where it does not exist, i.e. choice based on false hope. By offering such choices, Brody feels that a physician may in effect violate the patient's freedom to choose. J.Marta (personal communication) also emphasizes the importance of 'rationality of options' when assuring free choice. Baylis (1990) feels the doctor–patient relationship cannot be free of coercion, as it is natural for the patient to feel her care will suffer if she does not comply with the physician's perceived treatment plan for her. Sherwin (1994) further fears that offending the physician robs the patient of a true sense of control over her care. It is important to appreciate and understand these and other relationship issues (Kenny, 1995) prior to therapeutic prescription.

Specifically for reproductive medicine, relationships (woman–man, woman–family, woman–society) may motivate the martyrdom of the woman to sign consent for tuboplasty or other poor medical treatments, rather than accepting the alternative of adoption or focusing on other of life's beauties (Nisker, 1995). Katz Rothman (1987) explains the difficulty a woman compelled to have a child has in denying any reproductive therapy offered, as by denying the therapy she feels she has not done all in her power to achieve that child. I believe fear of carrying this society-inflicted guilt forever is a major force impelling a woman to accept a therapy with little chance of positive outcome. It is easier for her to satisfy the expectations of her husband, family members, and society in general, no matter what the risk, than to say 'I have other plans for my life, rather than accepting a therapy with such little chance of giving me a child'. Thus from the infertile woman's perspective, the offering of a therapy, even if the chance of a child is remote, becomes a further burden, a further proclamation from society's representative, the doctor.

Is it the moral duty of a physician to prescribe a low-rung therapy if the couple understands the chance of pregnancy morbidity and risk, and if it is the only therapy the couple can afford? Or is the physician's moral duty to avoid this therapy in order to protect the woman? Exploring the duty of the physician is extremely important, for the woman assumes by the physician's offer of a therapy, that the therapy has value regardless of how remote the chance of pregnancy, or how significant the morbidity or risk. For if the therapy has no value, her physician would never offer its possibility, would never allow her an unfounded risk, would never participate in the delivery of a valueless therapy. Even if the therapy is demanded by the couple as the only option affordable, the concerns of Baylis (1990) and Sherwin (1994) regarding power differential in informed choice, Brody's (1985) minimal success criteria and Marta's (1994) emphasis on rationality in decision-making, all question, for example, the offering of therapies other than DI or ICSI for severe sperm problems and therapies other than IVF for severely-damaged Fallopian tubes.

There has been a trend in the last two decades for couples to delay having children for social, academic, or professional pursuits (Baird, 1993). Unfortunately many women who delay pregnancy (especially beyond their mid-30s) find they have difficulty conceiving due to oocyte depletion (Bowman and Saunders, 1995; Daniel, 1995) or possibly endometriosis and tubal disease (Berkowitz et al., 1990) and will incur higher risks of spontaneous abortion and problems during pregnancy (Lansac, 1995). Regardless of these factors, couples on superior socio-economic ladder rungs can choose to delay child-bearing, confident of the capacity their money will have to buy the top-rung reproductive therapy that is required to obviate any fertility problem ageing may create. This confidence in wealth and medical science has already proved well-founded in the oocyte purchase programmes described above; and the future promises an unlimited supply of oocytes from oophorectomy and cadaveric sources, to be micro-injected with spermatozoa, forming hundreds of embryos, virtually guaranteeing children to wealthy couples.

In their security of wealth and science, a couple on a high societal ladder rung may continue their unencumbered youth's enjoyment, academic and professional pursuits, and ascend the socio-economic ladder until an acceptable height has been achieved before directing attention to having the child that will satisfy society's expectation. The accumulated financial
resources of this high-ladder-rung couple will allow significant support for the child, such as private school education, creative summer camps, travel, and the best employment opportunities, and access to high rungs on future reproductive therapy ladders.

In vertical societies, a woman confined to a low ladder rung cannot pursue a career in the complacency that her dreams of having a child will eventually be granted by modern medicine, rather she suffers the anguish of pregnancy procrastination with the hope that her Fallopian tubes remain pristine, endometriosis dormant and her own ovaries’ oocytes readily available. This peril provokes women to have children soon after marriage or indeed enter a couple unit largely for a procreative purpose. These couples may indeed achieve their goal of having children, but then see their children suffer the scars of parents labouring under oppressive economic and career pressures. Thus, the existence of reproductive therapy ladders, by compelling early pregnancy consideration, may contribute to the numbers of emotionally- and financially-deprived children, and thus perpetuate the next generation’s socio-economic ladders and the reproductive therapy ladders they will erect.

Why society accepts ladders
The willingness of a particular society to accept reproductive therapy ladders reflects the broader social issues in the country in which the ladder stands. Where ladders exist, the slope of the ladder represents the degree to which a social justice or autonomy imperative prevails in that society’s ethos. Autonomy-prevailing societies, such as North America, are likely to accept the 90° vertical ladders of reproductive therapy in Figure 1, while societies with greater dedication to social justice may insist on a lesser slope (such as the French full funding, except restriction to four IVF cycles and to couples in a relationship of a minimum of 2 years’ duration).

One reason vertical societies accept infertility treatment ladders (and other socioeconomic constructed ladders) is the perception that people ‘deserve’ or have the ‘right’ to have their feet on certain ladder rungs by ‘virtue’ of their work capacity, intelligence, or karma. This vertical society autonomy imperative is diametrically opposed to the social justice ethos of horizontal societies, where rights tend to be equally afforded to all members of society, purely on their membership.

For reproductive health care ladders, the inclusion of right to procreation (thus right to assisted reproduction) being encompassed within the right to optimal health care is an additional consideration. For example, in Canada, the universality of health care guaranteed by the Canada Health Act of 1979 never translated into provincial government funding of IVF, except in the province of Ontario. The social justice conscience of Canadians would never have accepted less than full funding for paediatric care, heart disease, organ transplantation, or hip replacement; but Canadians complacently accepted exclusion of optimal fertility treatment. Perhaps it is the reality of self interest, as most have not personally experienced denial of children, or have had no problem conceiving, or are not yet at the time of life when commencing a family receives consideration; or perhaps they are seniors more concerned that health care dollars remain available for the conditions imminent to them. The relatively small infertile constituency and their physicians have not been successful in promoting public outrage and positive political decision.

Chopping down ladders
Jacob’s ladder, strewed with angels, reached to heaven. There are no angels on Rachel’s ladders, rather socio-economic based therapies proclaiming whether perceived heaven will be reached. These therapy ladders in many countries are as steep as the socio-economic ladders that compelled their construction.

The first and most important role of health-care personnel in chopping down reproductive medicine ladders is to diffuse society’s sentence that women must climb these ladders, i.e. pregnancy should not be equated with heaven nor infertility treatment a life’s necessity. By being overly supportive, we inadvertently crystallize the concept that ladders must be climbed. It is our role to educate the population that most infertile couples will not achieve pregnancy no matter how high a rung the woman holds, so that women do not suffer the emotional ups and downs, do not fall into an emotional abyss in quest of a perceived pregnancy summit. To de-emphasize the societal inflicted imperative that women must bear children, we must explore the relationship issues that motivate the martyrdom of women to potentially dangerous therapies. To ensure our therapy is based on the patient’s aetiology rather than personal wealth, we must investigate the complacent delivery of health care based on socio-economic construction, and demand optimal care for all our patients.

Let us remove the blinkers that abrogate to political whim or economic viciusitude; our responsibility is to afford justice to vulnerable patients. Let us solicit support from professional organizations to demand moral delivery of reproductive medicine. Let us take positions to ensure that what we develop in our laboratories will be available to those of all financial fortunes and will be a benefit to society. Let us include in the duty of health care workers the altering of health care systems supporting ladders.

References

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