Towards less confusing terminology in reproductive medicine: a proposal

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This lead debate article is published simultaneously in this journal and in Fertility and Sterility with the aim of achieving the broadest possible response. Professor Habbema and co-authors, backed by both journals, wish to focus on achieving consensus on this topic. Readers are invited to submit well-argued response articles of up to 3000 words to either journal. These will be peer-reviewed and published as appropriate (but only in the journal to which they are submitted). At the end of 2004 it is hoped that these debate series will be one of the pieces of evidence used to establish consensus. Any agreed consensus document emerging in due course will be published in both journals.

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The use of the term ‘infertility’ and related terms in reproductive medicine is reviewed. Current terminology is found to be ambiguous, confusing and misleading. We recommend that the fertility investigation report of a couple should consist of statements concerning description, diagnosis and prognosis. The fertility investigation report forms the basis for further action, including the possibility of waiting with treatment in case of almost normal or only slightly reduced fertility. The use of the terms infertility, subfertility and fecundity is not necessary, and it is recommended to avoid them.

Key words: fecundity/infertility/prognostic grading system/subfertility/terminology

I. Background

Several nomenclature issues confront patients, clinicians and investigators in reproductive medicine.

1. Because the term ‘infertility’ covers disorders ranging from sterility to (nearly) normal fertility, its uniform application is misleading. By chance, even normal fertile couples may be included, especially if the period of non-conception is short.

2. No agreement exists on how long involuntary failure to conceive must continue to warrant use of the infertility designation.

3. Instead of infertility, often the term subfertility is used, covering more or less the same notion.

The terms fecundity and fecundability are also used in reproductive medicine, without being clearly defined.

A number of connected problems flow from these basic nomenclature issues. One outstanding example is the lack of agreement among health care providers on whether involuntary failure to conceive is a health care problem deserving insured coverage.

This paper attempts to summarize some fundamental terminology issues in order to facilitate discussion among clinicians, researchers and patients. The journals responsible for communication of medical care research in this subject are also key parties to such discussions. Furthermore, participation of the World Health Organization (WHO) would ensure that proposals emerging from the discussions might have a level of authority that could facilitate acceptance by governments.

II. The terminology problems

A. Reproductive medicine

A.1. The noun ‘infertility’ has different meanings, which can give rise to misinterpretation, errors in communication and confusion. Of course, the same problems arise with the related adjective ‘infertile’.

In common language (see Appendix) infertile and infertility have a root meaning of ‘not fertile’. They are equivalent to ‘impossible to conceive’, or ‘unable to have a child’ in the sense of sterile. By contrast, fertility is the actual production of live offspring and is the antonym of infertility (Last, 1988). These definitions suggest that there is a dichotomy of fertility and infertility without gradations in between.

Medical dictionary definitions improve on the general dictionaries, but raise new problems, for example Stedman’s
from `subfertility'.

From medicine journals. The use of two different terms might aid in Trials, and in all of the related high impact reproductive publications, abstracts of the Cochrane Database of Systematic human subjects in 2002. `Subfertility' was used in ESHRE `Subfertility' in 63 English language Medline citations on `infertility'. `Infertility' appeared as a subject word in 1046 and presumably to avoid the definition issues associated with Stedman's Medical Dictionary

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Medical Dictionary, 27th edn: `Infertility: diminished or absent ability to produce offspring; in either the male or the female, not as irreversible as sterility.' While this definition allows for a range of severities, it introduces a distinction between sterility (irreversible) and diminished ability to produce offspring (not irreversible). Although infertile populations invariably include some couples that will never conceive and are therefore sterile, follow-up to menopause would be required to determine the condition.

A.2. When there is no obvious cause after a diagnostic evaluation, the term `unexplained infertility' is used indicating the existence of an as yet unknown biological mechanism. This suggests that in the other diagnostic categories the cause of the infertility is explained, thus known. For example, the terms tubal infertility and male infertility suggest that the infertility is caused by tubal disease and a sperm disorder respectively. However, these apparent abnormalities may well co-exist with unknown biological mechanisms that are more influential than the apparent defect.

A.3. The terms ‘infertile’ and ‘infertility’ are also used in a descriptive manner to indicate the length of the delay in conception after starting regular unprotected intercourse, after stopping the use of birth control. This period of ‘infertility’ in the sense of non-conception theoretically can vary from 1 month to >35 years, but the clinically meaningful range is from 6 months to 5 years.

A threshold of 1 year to fulfil the definition of ‘infertility’ has become the gold standard for clinical purposes. (See for example definitions in C.M.March, Acquired intrauterine adhesions: Asherman’s syndrome; D.S.Guzick, Human infertility: an introduction; and R.S.Schenken, The treatment of infertility: the special case of endometriosis; all in Adashi et al., 1996). A threshold of 2 years, however, is used in many epidemiological studies: a WHO scientific group recommended the operational definition of primary infertility as: ‘the woman has never conceived despite cohabitation and exposure to pregnancy for a period of two years’ (WHO, 1975).

For comparability between clinical and epidemiological studies, this difference in thresholds can be misleading.

A problem causing much confusion is that this descriptive definition of ‘infertile’ has absorbed the ‘impossible to conceive’ connotation from common parlance. Consequently many patients and clinicians tacitly assume that after 1 year of ‘infertility’ the probability of conception is close to zero, which would justify immediate treatment.

A.4. The term ‘subfertility’, not included in either Dorland’s or Stedman’s Medical Dictionary, has been widely adopted, presumably to avoid the definition issues associated with ‘infertility’. ‘Infertility’ appeared as a subject word in 1046 and ‘Subfertility’ in 63 English language Medline citations on human subjects in 2002. ‘Subfertility’ was used in ESHRE publications, abstracts of the Cochrane Database of Systematic Trials, and in all of the related high impact reproductive medicine journals. The use of two different terms might aid in discriminating between different meanings of the term infertility, but no authority has made clear how ‘infertility’ differs from ‘subfertility’.

A.5. None of the dictionary definitions explicitly state that involuntary childlessness is a disease. Yet the American Society for Reproductive Medicine (ASRM) web site has the following definition of infertility: ‘Infertility is a disease**. The duration of the failure to conceive should be twelve or more months before an investigation is undertaken unless medical history and physical findings dictate earlier evaluation and treatment.’ [**Any deviation from or interruption of the normal structure or function of any part, organ, or system, or combination thereof, of the body that is manifested by a characteristic set of symptoms or signs, and whose etiology, pathology, and prognostic may be known or unknown. Dorland’s Medical Dictionary 1988: 481.”]

While this statement from the ASRM is unambiguous, there is reluctance to accept the designation of infertility as a disease among government and private health policy planners in many nations, for reasons that have not been made explicit. It is assumed that the high cost of various treatment options, which are often started too soon, and the low number of long-term outcome studies may influence such policy decisions. It may also be related to the many confusing and contradictory definitions used in reproductive medicine. Anyhow, when infertility is defined as 1 year without conception, calling this a disease at the same time is stretching the disease concept considerably.

It is better to consider the unwanted non-conception as the symptom for which the couple seeks healthcare. It is quite comparable with ‘upper abdominal pain’, ‘low back pain’, ‘fever’ or ‘sleeplessness’ in other clinical contexts. And, as in the other clinical situations, the clinician should find out whether the symptom likely reflects an unfavourable prognosis which requires treatment or more favourable prognosis in which a ‘wait and see’ policy is appropriate, and medical treatment is not yet needed. Note that, contrary to other medical conditions, non-conception is a ‘negative’ complaint in that the absence of something (i.e. a pregnancy) bothers the patient.

In summary, the terminology issues associated with the term ‘infertility’ include: (i) the unwarranted assumption that infertility approaches sterility; (ii) diagnostic statements are too easily interpreted as causal; (iii) uncertainty about the duration of delay that would justify the designation ‘infertile’, assuming that a single threshold could be useful for this purpose; (iv) the co-existence of two terms, ‘infertility’ and ‘subfertility’, that appear to have similar if not identical meaning. Approaches to the resolution of these issues should involve representation from interested academic, professional and international constituencies.

B. Demography and reproductive medicine

Terminology in demography has been influenced by the fact that demographers have originally worked mostly on data collected from registrations such as births or deaths. When observing the fertility of individuals or groups, the demographer counts the live births that occur in a given period of time. For example, a couple has been fertile in the first 2 years of marriage if at least one live birth is recorded during this period; if no birth has been recorded, the couple has remained infertile
over the same period. This has nothing to do with whether they wanted children or used birth control. It also has no implication for future fertility. For a group of individuals, the fertility rate over a fixed interval of time expresses the ratio of the number of live births to the total number of women or couples. The total fertility rate refers to the mean number of children a group of women had during their lifetime. The terminology has been published in a dictionary by the main international association of demographers, the International Union for the Scientific Study of Populations (IUSSP) (last edition 1982). For the definition of fertility and infertility see Appendix. In these descriptive definitions the demographer is concerned only with measuring results that can be observed. Consequently, infertility can be due to a deliberate choice of not having a child (voluntary infertility) or to some biological obstacles (involuntary infertility). We would recommend that ‘infertile’ and ‘infertility rate’ in this descriptive demographic sense is always used with a qualification of the period to which it refers. So, for example, ‘12 month infertility’ or ‘2 year fertility rate’. This type of qualification is even more pressing for those who continue to use the term ‘infertility’ in reproductive medicine despite our arguments, because when qualified to ‘x month infertility’ it is more precise and it better reflects the descriptive nature of the use of the term.

By contrast, the terms fecundity or fecund refer to the reproductive capacity. It would apply for example to a woman who is able to conceive if exposed to unprotected intercourse. The opposite of fecund is infecund or sterile. See Appendix for the IUSSP definition: the terms fecund and infecund are close to the terms fertile and infertile in common language.

Finally, the term fecundability means the probability of conceiving during a normal menstrual cycle given unprotected intercourse. So, fecundability measures the degree of fecundity. Fecundability depends on the timing and frequency of coitus and on biological parameters. It may apply to all conceptions or only to those that result in live birth.

Medline does not have fecundity as a MeSH term but associates the word with fertility. Fecundity appeared in 229 English language Medline citations during 2002, and fertility in 705. Interestingly, the term fecundability, which appears neither in Stedman’s Medical Dictionary nor in the Oxford English Dictionary, was found in 204 English language Medline citations during 2002.

Thus, the term fecundity is defined differently by scientific disciplines (epidemiology and demography on one hand and reproductive medicine on the other). Also, the reproductive medicine definitions have not been adopted by a widely accessible reference such as a medical dictionary.

III. Relevant aspects of reproduction

Reproduction is a matter of chance depending on the subtle balance between success or failure of complex, mostly poorly understood, sequential processes that may lead to a pregnancy and eventually to the birth of a healthy child. These processes include spermatogenesis and oogenesis, folliculogenesis, ovulation, sexual intercourse and transport of gametes, fertilization, migration of the embryo to the uterus and its subsequent implantation, and finally intrauterine development of the fetus. Failure can occur at any link of this delicate chain, but most commonly does so at the early stages. With regular unprotected intercourse, a new chance of pregnancy arises every menstrual cycle. Demographic studies show that the distribution of the monthly pregnancy chance of couples trying to conceive is heterogeneous.

Each couple has a more or less constant monthly probability of conceiving, but between couples the probabilities vary widely, from 0% to an estimated upper limit of ~60% (Léridon and Spira, 1984). A monthly chance of zero corresponds to fertility, which occurs in 3–5% of all couples (Greenhall and Vessey, 1990).

With a high monthly pregnancy chance, the average time to pregnancy is short, and vice versa. Hence the length of time in which couples have been unsuccessful at conceiving is an essential estimate of the degree of infertility.

If the unproductive period is short (for example, ≤12 months), the probability of future success is still considerable. When couples consult a physician after 12 months because no conception has occurred, their likelihood of conception without treatment will depend on their age, on whether they have had a prior conception, and on the results of diagnostic tests. The prospect for conception without treatment varies from hopeless, in the case of tubal blockage or azoosperma, to very good in healthy, young couples with normal or near normal test results.

Therefore, decisions about treatment for infertility depend initially on the likelihood of conception without treatment and it stands to reason that the definition of infertility should incorporate this likelihood in some way. Of course treatment decisions also depend on whether there is a treatment that works (has proven effectiveness), is worth using (has proven cost-effectiveness), and has a positive balance between chance of success and risks involved.

IV. A proposal

Terminology in medicine should be lucid, understandable, consistent and unambiguous. The technical meaning of each term should correspond closely to what is generally understood by ordinary people, thus excluding confusion between patients, clinicians and researchers. The present proposal attempts to disentangle the different aspects of the currently used terms infertility and subfertility. To avoid further confusion, we propose that these terms should no longer be used.

The fertility investigation report of a couple should be summarized in three types of statement: 1. descriptive or observational statement; 2. diagnostic or causal statement; 3. prognostic or predictive statement.

1. Descriptive statement

The descriptive statement concerns the non-pregnancy experience and only requires establishing the time from the start of unprotected intercourse until the time when first consulting a doctor because of involuntary childlessness. It would simply take the form of x months of non-conception while using no
contraceptive methods. It is purely descriptive, like the demographic term infertility.

Second, the descriptive statement also includes information on the age of the women and on whether this couple ever had a pregnancy before (secondary) or not (primary).

2. Diagnostic statement
After the first consultation, the couple will be offered a diagnostic work-up to obtain essential information on the previous history and the present situation of the female and the male, also by performing some diagnostic tests. Thereafter, a diagnostic statement can be made, which should be as causal as possible. Examples of some diagnostic statements are: ‘the x months primary non-conception period in this couple is related to ovulatory problems, tubal obstruction or sub-optimal sperm’ or other specific terms. For some couples the diagnostic statement would be ‘not related with any detectable barrier to conception’. The diagnostic statement should always include the descriptive statement.

3. Prognostic statement
After the diagnostic work-up, decisions have to be taken with regard to further action. For this purpose, a prognostic statement regarding the spontaneous probability of conception is necessary. We propose the following system of ordered prognostic categories: Grade 0: (almost) normal fertility; Grade 1: slightly reduced fertility; Grade 2: moderately reduced fertility; Grade 3: seriously reduced fertility; Grade 4: sterility.

The prognostic statement is a clinical judgement based on the information obtained, including the duration of non-conception, the age of the female partner, the cycle characteristics, whether the involuntary childlessness is primary or secondary, and on the results of the diagnostic tests performed. It is based on the estimation of the physician, and should be made as explicit as possible. The most important question to be answered is whether treatment is already warranted or whether the couple should be encouraged to wait and try to realize a spontaneous pregnancy themselves. Therefore, the prognostic statement should be restricted to the chance of conceiving spontaneously within the following year. Because these chances are quantitative on a scale from 0 to 100%, it is important to establish the numerical probabilities to which the chances are quantitative on a scale from 0 to 100%. It is based on the estimation of the physician, and should be made as explicit as possible. The most important question to be answered is whether treatment is already warranted or whether the couple should be encouraged to wait and try to realize a spontaneous pregnancy themselves. Therefore, the prognostic statement should be restricted to the chance of conceiving spontaneously within the following year. Because these chances are quantitative on a scale from 0 to 100%, it is important to establish the numerical probabilities to which the chances are quantitative on a scale from 0 to 100%.

Some prognostic models (Eimers et al., 1994; Collins et al., 1995; Snick et al., 1997) may help the clinician to make these prognostic statements less subjective and more precise. But even without such models, the clinician should also try to classify the prognostic categories.

The fertility investigation report forms the basis for further action. In general, the clinician is likely to advise the couple to wait when the chance of spontaneously conceiving within the following year is still good (categories ‘almost fertile’ and ‘slightly reduced’). When there is an appropriate mode of treatment, this will be advised without any delay in the categories ‘seriously reduced’ and ‘sterility’. More reflection and counselling is required in case of ‘moderately reduced fertility’ (Grade 2).

The descriptive (1), diagnostic (2) and prognostic (3) statements for one couple should always be combined. Three brief cases are presented; for all three the age of the female partner is 30 years.

Case 1:
1. Thirty-six months primary non-conception
2. Bilateral tubal obstruction

Case 2:
1. Twelve months secondary non-conception
2. Slightly impaired sperm quality
3. Grade 1.

Case 3:
1. Fifty months primary non-conception
2. Non-conception is unexplained
3. Grade 3.

Most clinicians would agree with the prognostic classification given for these couples: Grade 4 (sterility) for case 1; Grade 1 (slightly reduced fertility) for case 2; and Grade 3 (seriously reduced fertility) for case 3.

In conclusion, it is possible to use a fertility investigation report that avoids the confusing terms infertility, subfertility and fecundity. A report should consist of statements concerning description, diagnosis and prognosis. For prognostic purposes, a grading system is proposed.

Appendix: Dictionary definitions of fertility, infertility and sterility in common language and in demography

English dictionaries

Oxford English Dictionary
infertile = 1. unable to reproduce. 2. unable to sustain crops or vegetation (of land).
American Heritage Dictionary
infertile = 1. not fertile; unproductive or barren. 2. incapable of producing offspring; sterile.

Concise Oxford Dictionary of Current English
fecund: prolific, fertile
fertile: bearing abundantly, fruitful
infertile: not fertile

Cobuild English Language Dictionary (Collins, London and Glasgow, 1987)
infertile 2. a person or animal that is infertile is unable to have or to produce babies.
infertility is often considered a synonym of sterility.

French dictionaries
In French dictionaries (Larousse, Robert), ‘Fécondité’ means clearly the ability to reproduce, bear children, etc. It is more or less synonymous with ‘fertilité’. The opposite of ‘fécondité’ (or of ‘fertilité’) is stérilité.

Multilingual Demographic Dictionary (IUSSP, Liège, 1982)
–623 Fertility and infertility refer to reproductive performance rather than capacity, and are used according to whether there was actual childbearing or not during the period under review. Permanent infertility may extend from a certain age or marriage duration to the end of childbearing years.
–621 The capacity of a man, a woman or a couple to produce a live birth is called fecundity. An alternative of the term fecundity implies the ability to conceive, rather than to produce a live child. Terms sub-fecundity and sub-fecund mean either that the capacity to produce a live child is below normal, or that the probability of conception is low. The lack of that capacity is called infecundity or sterility; inability to conceive is the main, but not the single, cause of sterility. Used alone, sterility usually carries the connotation of irreversibility, but occasionally temporary sterility is distinguished from permanent sterility. Among women we distinguish primary sterility where the woman has never been able to have children, and secondary sterility, which arises after one or more children have been born.