of mathematical and statistical jargon. Rest assured however, that this letter will not contain any details of statistical methodology, but will simply make some general, but rather important, remarks on the topic of the interpretation of research data.

In this journal (Walters, 1991, 1993, 1995), and elsewhere (Walters 1994a,b), I have pleaded for a more responsible application of statistical methodology in assisted procreation research. A less than completely fastidious use of the subject is sure to lead to erroneous inferences resulting in controversies such as the present one relating to oral contraceptives.

Inferences from research data are frequently based on a probability value which provides evidence of the effect of some important factor. In calculating this probability value however, the analyst needs to make several assumptions about the selection of the experimental material (patients, oocytes, embryos?), the allocation of the treatments, and the population of interest, in addition to assumptions relating to the numerical procedure adopted. Unfortunately, these validating assumptions are ignored completely by many research workers and very few published papers in our subject are founded on really sound statistical principles.

The foundations of good statistical practice were laid down many years ago, but in recent times it seems to have become fashionable to devalue or indeed disregard completely these sound principles. For example, randomization, which is such an essential part of objective evaluation, is now hardly ever applied. One result of this erosion of standards is that papers are often published which, although citing a probability value in support of inferences, also contravene virtually all the precepts of good statistical practice, thus making the inferences valueless.

Whereas it is absolutely imperative in many branches of medical research to examine vast quantities of retrospective data in order to make progress, the analyst should not be deluded into thinking that this is an alternative to a carefully-controlled prospective randomized study, where the aims are clearly stated at the outset. As far as assisted procreation is concerned, where a good deal of the effort is in the private sector, I fear that it is rather difficult to achieve complete, disinterested, objectivity. The European Society for Human Reproduction and Embryology (ESHRE) could surely play an important role here in promoting and possibly supporting prospective investigations to study some of the more intractable problems in assisted reproduction technology.

Although I agree with virtually all the points made by Cohen (1996) in his aptly entitled note 'Epidemiological Disasters', I must take issue with his final sentence which gently derides the efforts of, amongst others, 'mathematicians of medicine'. Until researchers realize fully the limitations of the retrospective epidemiological study, and give proper value to the rigorous prospective randomized investigation, epidemiological disasters will be a regular feature of research.

Unfortunately, statistics has now acquired the image of a 'number juggling' discipline, but it needs to be remembered that statistical inference is in reality a branch of philosophy and scientific method. The worst abuses of the subject are not due to poor 'number juggling' but rather, poor science, and muddled inferential philosophy.

References
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D.E.Walters
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Dear Sir,

I fully agree with Dr Walter's comments. Who could do otherwise? But, alone, they do not solve the dilemma we face in relation to the analysis and interpretation of risks in our field.

I wish to raise the question with Dr Walters of how we cope with epidemiologists today. It is essential that statisticians and analysts, such as he, can alert us to the ambiguities and concerns arising with new advances in our field. We poor clinicians need this help! Most of us find epidemiological studies to be highly numerical, and we are unable to analyse conclusions drawn by such analyses. Besides, the epidemiologists themselves quarrel amongst each other, which does little to improve our understanding. They question statistical interpretations of many studies and in turn face their own critics. Disputes thus arise over the historical aspects of apparently well-established studies, a problem I have referred to before.

Consequently clinicians have had to suddenly face a series of new doubts and questions on several important aspects of their practice in their field of work. Cancer of the breast and contraception, gonadotrophins and cancers of the ovary are but two recent examples. Clearly we must avoid any more such sudden confrontations from committees or experts!

I would like to conclude by making a simple recommendation. It is necessary to propose a combined meeting of epidemiologists and clinicians about a potential threat to health before it is published in the media. If we do not act in this way, or in some similar manner, a dictatorship of epidemiologists quoting figures, which may or may not be
Correlation between testicular histology and outcome after intracytoplasmic sperm injection using testicular spermatozoa

Dear Sir,

This is with reference to the article by Tournaye et al. (1996) on the correlation between testicular histology and outcome after intracytoplasmic sperm injection (ICSI) using testicular spermatozoa.

Since a pregnancy has been reported after ICSI of spermatids (Fishel et al., 1995) could the authors please review their findings, and let us know whether any spermatids were observed in the wet preparation of those patients in whom no spermatozoa could be found for ICSI? If spermatids could in fact be found, then there would be no need to resort to using donor spermatozoa.

We recently had a patient with undescended testes (histology reported as incomplete maturation arrest), for whom we attempted a testicular sperm extraction (TESE) with ICSI. In spite of taking four biopsies from both the testes, and searching for 4 h, we could not recover any spermatozoa. We were forced to resort to using spermatids (which, incidentally, were present in abundance) for ICSI. Of 12 oocytes injected, four showed 2 pronuclei 18 h after ICSI. Only one of these cleaved to form a fragmented 4-cell embryo, which was transferred into the Fallopian tube. Unfortunately, a pregnancy did not result.

Three out of these five patients showed an arrest at the spermatocyte level, while the two other patients showed an arrest at the spermatid level.

For Dr Malpani's interest, I updated our series: of the 70 patients showing a maturation arrest pattern at testicular histopathology, testicular sperm recovery failed in 31 (44%). In one of these patients an arrest at the spermatogonial level was observed. In all, 25 patients showed a maturation defect in meiosis and the other five patients had a defect in spermiogenesis. It is also interesting to mention that in 27 patients in whom histopathology had shown an arrest at the spermatid level, spermatozoa could be successfully recovered in 22 cases (81.5%) thanks to multiple testicular biopsies with wet preparation.

We are aware of the recent case reports on spermatid injection (Fishel et al., 1995; Tesarik et al., 1995, Vanderzwalmen et al., 1995). In our updated series of patients undergoing testicular sperm recovery because of azoospermia associated with maturation arrest, these techniques may have been beneficial for five patients (7%). So far, we have not performed spermatid injection techniques in these patients, since in our experience it is sometimes difficult to distinguish whether the spermatogenic cell is haploid or diploid, and we feel that there may be a substantial risk of microinjecting a diploid cell. Therefore, we are conducting further research in order to improve the feasibility and safety of this technique before implementation in our clinical setting. We hope that other researchers will provide more non-casuistic information on the feasibility and safety of the different spermatid injection procedures.

References


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Dear Sir,

We appreciate the interest Dr. Malpani has expressed in our recent paper (Tournaye et al., 1996).

In response to his comment we would like to clarify that of the 18 patients showing a maturation arrest pattern at their testicular histopathology, five had no intracytoplasmic sperm injection (ICSI) as no spermatozoa were available for microinjection.