

Dr. Ricardo Asch. My point was that he was still innocent since he had not been charged with any offense. I also stressed that he had been a close and trusted colleague and friend, and had done all he could to respond to call made on him during joint research work or as an editor.

5. I feared that the outlook seemed to be very dark for Ricardo, and that it would be a desperately sad day for me if a legal judgment went against him.

These points were made in the lecture, I still adhere to them today and wish to stress that this letter states my position exactly.

Professor Robert G. Edwards, M.D.  
Editor, Human Reproduction  
Cambridgeshire  
United Kingdom  
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**Editorial Comment**  
**High-Resolution Map for Assisted**  
**Reproductive Technology**

*The birth of Baby Louise was a creative peak for infertility treatment, but no one could have anticipated the subsequent influence of this technology on attitudes and practices related to human reproduction. The technology of assisted reproduction (ART) clearly provides solutions to many problems of male and female infertility, but it is also one of reproductive medicine's principal problems. It has added to the cost of infertility treatment and sometimes impersonalizes the surroundings in which that care is delivered. Only a few anticipated the widespread embellishments and commercialization of this technology that has swept the United States and other countries. Professor Robert G. Edwards in his recent Herbert H. Thomas. lectureship at the 1995 meeting of the American Society for Reproductive Medicine reviewed certain historical, current, and future 'aspects of assisted reproduction. This was a unique lecture because it came from the individual most responsible for the development of human in-vitro fertilization (IVF). He pointed out some of the interesting highs and lows that have been part of this technology over the past 10-15 years. Some of the lows such as the perversions and misuse of probability statistics are a little bit like comedy with a scientific tinge. Others as reiterated by Professor Edwards in his letter are more tawdry and invariably suggest a more negative view of humanity in general. They indicate that a moral compass is badly needed for precise navigation and legal protection of patients. Without such a com-*

*pass the invariant improprieties of a few will tarnish the efforts, commitment and dedication of other professionals in this field. The first step to implement an appropriate type of oversight might be the creation of a commission similar to the British Human Embryology and Fertilization Authority. Without such an authority it is doubtful that time alone, the mere manipulation of words or even stretching a few DNAs will make a "sow's ear into a silk purse".*

*A positive scientific note in Professor Edward's lecture was a single slide of an electrophoretogram demonstrating the use of 6 tetranucleotide microsatellite sequences as primers to determine the DNA profile of the embryo in order to exclude contaminating material. This figure published by the group in Leeds points out the important safeguards that must be in place if one is to perform embryonic DNA diagnosis with consistency and accuracy. (1) In addition to these scientific caveats Professor Edwards stressed the accurate reporting of IVF statistics. One cannot afford to be economical with the truth, when the stakes are future lives. His thoughtful lecture defines a time to move on to a new level of accountability.*

Paul G. McDonough, M.D.,<sup>1</sup> Edit&-Letters

REFERENCE

1. Findlay I, Urquhart A, Quirke P, Sullivan K, Rutherford AJ, Lilliford RJ. Simultaneous DNA "fingerprinting", Diagnosis of Sex and Single Gene Defect Status from Single Cells. *Molecul Hum Reprod* 1995;10:1005-13.

**Quinacrine Sterilization in the United States?**

To the editor:

The paper by Sokal et al. (1) offers two unsubstantiated conclusions: the single case of uterine sarcoma found in their study may make it difficult to license quinacrine for female sterilization in the United States and (2) even if approved, would probably not become widely used in the United States because of its relatively low effectiveness compared with surgical sterilization.

These unsubstantiated conclusions are most unfortunate because they will serve to discourage funding of further research by U.S. foundations and government agencies. Uterine sarcoma is a rare cancer. Their own analysis showed that, when compared with data from nine U.S. cancer registries, "These

[the number of expected uterine leiomyosarcomas] are not significantly different from the one case observed [in this study]." Why should a single case make it difficult to license this method?

The authors, without consulting American women, have concluded that they will not want to use this method. There are already many arguments against such a position. Nearly 100,000 women in 15 countries are now using this method. More than 12,000 women in West Bengal, India, have foregone a substantial government incentive (nearly 2 months' family income) to get a free surgical sterilization and chose to pay US \$4 (more than 2 weeks' income) to purchase a quinacrine sterilization in the private sector. Women in Namha Province, Vietnam, elected this method over surgical sterilization 11 to 1. Many American women probably would prefer the quinacrine method for the same reasons as their Indian and Vietnamese counterparts.

The U.S. Food and Drug Administration (FDA) is concerned that quinacrine is a mutagen, and some mutagens increase the risk of cancer, even though quinacrine is an approved drug. It is estimated that the necessary FDA studies will require 10 years and cost over \$10 million. No pharmaceutical company is interested because of the poor patent position.

Should this method interest U.S. foundations and government agencies? There are hundreds of thousands of American women who want to be sterilized, are not eligible for Medicaid, but cannot afford \$2000 to \$3000 for the surgical procedure. The financial and social costs of the unwanted pregnancies resulting from, their inability to pay for this operation are enormous. Furthermore, more than \$1.5 billion is spent each year in this country for female surgical sterilizations. The cost of the same number of quinacrine sterilizations would be \$75 to \$150 million. The \$10 million price tag for the required FDA studies is minuscule when compared with the potential savings.

*Elton Kessel, M.D.  
Department of Public Health and  
Preventive Medicine  
Oregon Health Sciences  
University  
Portland, Oregon*

*Stephen D. Mumford, Dr.P.H.  
Center for Research on  
Population and Security  
Research Triangle Park  
North Carolina  
November 2, 1995*

## REFERENCES

1. Sokal DC, Zipper J, Guzman-Serani R, Aldrich TE. Cancer risk among women sterilized with transcervical quinacrine hydrochloride pellets, 1977 to 1991. *Fertil Steril* 1995;64: 325-34.

### *Reply of the Authors:*

In our article (1), we gave a guarded assessment of [1] the possibility of quinacrine's approval by the U.S. Food and Drug Administration (FDA) and [2] its likely popularity among American women. We did not intend to discourage further research on quinacrine as Kessel and Mumford fear, but believed that we had to describe clearly its limitations. As Kessel and Mumford suggest, the use of quinacrine pellets to occlude the Fallopian tubes may have some potentially important advantages compared with surgical sterilization, including short-term safety, ease of administration, and low cost. A recent review (2) notes these potential advantages, but also notes the limitations of current research.

Regarding the implications of the single case of uterine leiomyosarcoma that we reported, the FDA proposed recently that researchers prepare a worst-case analysis in assessing adverse events (3). The worst-case analysis for leiomyosarcomas after quinacrine use would be about a 10-fold increase in risk. Even though uterine leiomyosarcoma is rare, it is usually fatal, and a potential 10-fold increase in its incidence could well pose a serious obstacle to FDA approval. Another issue that the FDA might raise is the risk of ectopic pregnancy. Family Health International is conducting a long-term follow-up study of women in Vietnam to gather additional data regarding this issue.

Regarding quinacrine's likely acceptability among American women, a major limitation is its lower efficacy among women <35 years. Long-term follow-up data from Chile show cumulative life-table pregnancy rates of approximately 10% at 10 years in women who received quinacrine pellets before the age of 35 years (2). Efficacy is better in women ≥ 35 years, with a cumulative pregnancy rate of approximately 3% at 6 years, probably because of the decreasing fertility of older women.

Women < 35 years clearly have better reversible contraceptive alternatives, including IUDs such as the copper T (TCu380A) or the levonorgestrel-releasing IUD (LNG-IUD; Leiras Pharmaceuticals, Turku, Finland), and injectables such as depo-medroxyprogesterone acetate (DMPA or Depo-Provera; The Upjohn Company, Kalamazoo, MI). While the LNG-IUD is relatively expensive and is not yet available except in a few developed countries, both the

TCu380A and DMPA are inexpensive and widely available.

Kessel and Mumford point to quinacrine's acceptance by women in developing countries. However, many of these women may have had limited contraceptive choices and may have chosen quinacrine because of a fear of surgery or lack of access to surgical methods. These factors would be less important in the United States.

*David C. Sokal, M.D.  
Family Health International  
Research Triangle Park, North Carolina*

*Jaime Zipper, M.D.  
Sotero del Rio Hospital  
Area Sur Oriente  
Santiago, Chile*

*Rene Guzman-Serani, M.D.  
Universidad Austral de Chile  
Valdivia, Chile*

*Tim E. Aldrich, Ph.D.  
Department of Epidemiology  
University of North Carolina  
Chapel Hill, North Carolina  
November 27, 1995*

#### REFERENCES

1. Sokal DC, Zipper J, Guzman-Serani R, Aldrich TE. Cancer risk among women sterilized with transcervical quinacrine hydrochloride pellets, 1977 to 1991. *Fertil Steril* 1995;64:325-34.
2. Sokal D, Zipper J, King T. Transcervical quinacrine sterilization-clinical experience. *Int J Obstet Gynecol Suppl.* In press.
3. Food and Drug Administration. Adverse Experience Reporting Requirements for Human Drug and Licensed Biological Products (Proposed rule). *Federal Register*, October 27, 1994;59:54046-64.