In the past 24 years, more than 130,000 women in 31 countries have undergone the quinacrine pellet intrauterine sterilization procedure. This technique, with its unquestionable safety, simplicity, good efficacy, and low cost, has primarily been offered in third world countries. Both the IFFH (International Federation for Family Health) and FHI (Family Health International) have endorsed research into this method. Nevertheless, fierce opposition from certain quarters has led several countries to suspend their programs. It is only within the last four years that three American advocates, all internationally respected scientists, began to focus efforts to bring the method into the mainstream of reproductive control choices in the United States.

In 2000, the U.S. Food & Drug Administration (FDA) approved an investigational new drug (IND) trial application to clinically evaluate QS in American women. Some detractors still insist on expensive and time-consuming animal research before using women as subjects. Other investigators, among them Malcolm Potts and Giuseppe Benagiano, have stated these “cannot prove human safety.” They also observed that such animal tests can produce results “qualitatively different from those subsequently found in humans, as occurred with Depo-Provera” (1). It is interesting to note that for many years, the World Health Organization (WHO), under the direction of Dr. Benagiano, opposed QS. In the above commentary, the authors note a cumulative low risk of serious, immediate side effects, but insufficient data to answer questions about potentially important, long term side effects. They are glad FDA trials are underway, but while admitting the safety answer lies in “a very large scale of controlled use”, they cautiously advise offering QS only to women who “present unacceptable risks.” A very conservative and limiting “middle road!”

Dr. Jack Lippes, inventor of the famed Lippes Loop Intra-uterine Device (IUD), has recently completed a phase one trial of 10 women, and a national trial is expected soon.

The U.S. FDA Modernization Act of 1997 Pharmacy Compounding Provisions became effective November 21, 1998. This enabled American physicians to offer QS to their private patients with individual prescriptions filled by compound pharmacists.

Quinacrine hydrochloride is a yellow dye and antibiotic manufactured in powder form for medical usage. It has been available since the 1920s and was used extensively in oral tablet form as an anti-malarial prophylactic and treatment in the U.S. service men and women during World War II (as much as 36,500 to 52,000 mg per person). A great deal of research on its oral usage has shown it to be very safe in doses under 3000 mg per month; millions of American and foreign children have taken the drug for the intestinal parasite, Giardia, and it remains the only FDA approved drug for this purpose. Doctors around the world continue to use it for these and other medical conditions such as lupus and tapeworm. Unfortunately, the drug’s manufacture in the U.S. was discontinued in the mid 90s, and our FDA has refused to allow the importation from a Swiss manufacturer of previously inexpensively made Q pellets for the sterilization procedure. Thus, at present, the powder must be imported and “compound” pharmacies are then able to laboriously make much more expensive pellets for the
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IUD-like insertion process. Dr. Stephen Mumford, Dr.P.H., president and director of the Center for Research on Population and Security, one of three noted American scientists advocating QS, is the supplier of the pellets for international trials.

What is the history of the QS method and how does it work?
The QS method was developed in Chile in the late 70s by Dr. Jaime Zipper, the inventor of the Copper T IUD, and after some trial and error, the optimal dose for trans-cervical insertion of the pellets was found to be 252 mg in seven pellets ejected from the modified copper IUD inserter high in the uterus about .5 to 1 cm from the fundus with the sheath held steady at that depth. This must be done twice in consecutive months and in the week following a menses. If the woman is using the depo-mpa method of contraception, which may enhance the success of the technique, there may be no menses to guide one. It is important to the success or efficacy that there be no blood in the uterus, as this interferes with the action of the quinacrine. Concentrations of quinacrine in the uterus after insertion are higher than for oral administration for only a matter of a few hours, but they are adequate to cause a significant chemical endometritis from which the thick endometrium always recovers. However, with proper flow into the proximal tube where the mucosal lining is only a single cell thick, recovery is unlikely and scar tissue “plugs” develop to obstruct any future access of sperm to ovum.

Regarding my practice, in which I have sterilized five women with quinacrine, I wish to make a few brief points:

1. Sedation before insertion is unnecessary, but one might wish to do an anterior cervical lip anesthetic injection for the tenaculum (I use a sharp toothed one), or an atraumatic instrument.

2. Be certain of the position of the uterus in the body in the initial bimanual pelvic exam. When sounding to the fundus, try a gentle rotation or side-to-side motion of the sound to see if there might be a septum. I suspect some of our failures may be due to a partial septum, which I have found in my OB/GYN career to be not uncommon; this might deflect much of the quinacrine liquid to one side.

3. Immediately after insertion, the woman should lie down on a couch or bed so as to maximize the uterine fundal position downward. We are experimenting with a long foam wedge to facilitate this and hopefully make more of the quinacrine available to the cornuae.

4. After 30 minutes, one can see thru a reasonably full bladder with ultrasound whether there is quinacrine flow to the cornuae. There is new 3-D technology which can better define the extent of the developing scar.

5. With the second insertion, one may encounter some immediate cervical bleeding on sounding, probably a residual of the quinacrine inflammatory effect of the previous pellets. I do not consider this a contraindication to continuing with the insertion.

I have extensively advertised the method in telephone yellow pages, on the Internet at my website, by making copies of my introductory brochure available to nearby clinics, and by mail to any interested callers. My fee is $500 USD, which may seem high to many of you, but I assure you I am not even close to breaking even yet with my expenses. I also offer a payment plan. My cost for the package of two sets of pellets and inserters is about
$150, which I require in advance. The five women, ranging in ages from the late 20s to the early 40s, have tolerated two insertions very well, with minimal side effects, mainly low back and/or abdominal ache; none have required pain medications, had fever or headache, or missed any daily activities, such as work, afterwards. All have been Caucasian without insurance coverage. They have been extremely pleased with the method. I will continue to follow them at six month intervals.

Questions asked of them recently have produced negative responses about:

1. Adverse menstrual changes such as a missed period followed by a heavy/crampy one (which could be and early miscarriage)
2. Sexual discomfort
3. Any changes or abnormal feelings in the abdomen.

I use IFFH sterilization register and follow up to record my cases, and have developed my own office protocol for calls and workup, history and physical exam forms. My consent form is extensive and only slightly modified from that developed by Dr. Mumford and others. I have Spanish translations of everything, including a training manual for providers.

Risks and the Opposition

Follow up of ten or more years post-sterilization will yield valuable information about reservations of many of the method's detractors. They express concern about increased likelihood for cancer, ectopic pregnancy, and birth defects in any subsequent pregnancies. We know of none of these risks with oral consumption of the drug -- at much higher doses than used in the sterilization process -- and pathology studies suggest that if the quinacrine reaches the Fallopian tubes, it closes them completely.(2) The risk of ectopic pregnancy following failure of surgical sterilization in the U.S. is higher than for QS, using newer insertion technique. Every year in my country, there are about a dozen deaths and about a thousand hospitalizations from complications of surgical sterilization. There has never been a death recorded with the QS pellet method -- a remarkable safety record. This includes rare cases of uterine perforation with the inserter and depositing the pellets in the peritoneal cavity. Although painful, once Q is absorbed, pain diminishes and there are no other sequellae. (3)

Antagonists make much of the fact that quinacrine is a mutagen (so is tetracycline) and would have others believe such drugs can cause cancer because of this factor. Direct evidence of quinacrine carcinogenicity in humans or animals has never been established. Finally, the drug does not appear to be terratogenic. In a 31,781 case Vietnamese trial, “there were two cases of quinacrine insertion during early pregnancy. One was a case of ectopic pregnancy, and the other woman gave birth after the study cut-off date. The infant was normal.” (4) There are some animal data for both monkeys and rats showing that exposure of the fetus at the time of embryogenesis leads to resorption or abortion, especially in early gestation, but there was no evidence for treatment-related malformations. (2)

An organization calling itself "Reproductive Health Technologies Project" published a negative statement last year on QS research status, even questioning the need for nonsurgical methods of sterilization. But the level of unmet need for contraception is rising rapidly. To satisfy the U.N. median variant population projection of 12 billion
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people at the end of the 21st century, we must achieve by 2035 a replacement fertility rate of 2.1 children per woman. The UNFPA estimates that this will require 200 million sterilizations in the 10 years ending in 2005, or three years from now. About 85% of these were projected to be female, the rest vasectomies. Given this situation, it is obvious that there is urgent need for a safe, effective, inexpensive method of sterilization that can be delivered by paramedical personnel in rural areas. (5) QS may be the answer, and a wide, controlled clinical study with good patient information and consent, combined with a parallel, retro-study of previous patients mentioned above, should be implemented immediately. In the U.S.A., our society's litigious nature will be a severe restraint unless or until the FDA gives its seal of approval to this remarkable method. Meanwhile, Dr. Mumford and others have been informing clinicians about QS at their professional meetings. The response has been gratifying. All ingredients in the pellets already meet FDA standards as does the sterilization process of pellets and inserters.

It is time for QS to be made available to women everywhere. I hope you will join us in offering it to them.

Thank you.

References:

3) Jack Lippes, M.D.: Quinacrine sterilization safety and efficacy. American Public Health Association annual meeting, Chicago, IL. November 8, 1999