

Quinacrine: Of Medicine, Politics, and Vested Interests - Where is the Woman in the Equation?

There is a fascinating story about a drug most of us have never heard of:

Quinacrine. Almost predictably, it is the story of a drug used widely and safely for decades but suddenly controversial when used to control fertility. And, guess what? Amid all the debate between UN agencies, international health officers, private researchers and medical politics, the woman patient is essentially ignored.

Quinacrine (first developed in the 1920's) might be familiar to World War II vets, for thousands of troops in the Pacific took a tablet a day as an anti-malarial prophylactic, amounting to 1,000 mg quinacrine/week. It was also used to treat active malaria, using larger doses (2,800 mg/week). Although long since replaced by other anti-malarial drugs, its importance in wartime generated 20,000 scientific papers on its safe use against malaria.

In fact, quinacrine is still prescribed for an odd assortment of medical conditions. It is given orally as a treatment for tapeworm and Giardia, an intestinal parasite. It has been used in connective tissue diseases like lupus. And because it has the capacity to induce scarring, it can be actually be painted on collapsed lungs to adhere them to the inner pleural cavity or can be used in advanced cases of lung cancer to prevent pulmonary fluid build-up.

Quinacrine's capacity to induce scarring prompted a different research project in Chile in the 1970's. When introduced into the uterus in liquid form, it caused scarring of the Fallopian tubes, amounting to a "medical" sterilization, as opposed to a surgical one. Because the fluid leaked out of the uterus and the scarring was often incomplete, the protocol was changed to inserting pellets of the drug. Over the years, small clinical trials of quinacrine as a female sterilizing agent were mounted in 13 countries of Asia, the Middle East and Latin America.

Then Vietnam undertook a very large

field trial in 1989. As a developing country, Vietnam has barely adequate medical facilities, a budget which assigns only 20¢/woman/year for family planning, and a rapidly expanding population. There is a backlog of over 7 million women wishing to be sterilized (the most common method of contraception in third world countries), but few can afford the hospital costs and not all wish to face the high number of medical complications following laparoscopic surgery.

Hence, the possibility of an effective non-surgical sterilization technique was attractive. In all, 3 1,781 procedures were done over a period of three years: 7 pellets of quinacrine (252 mg each) were placed high in the uterus with an IUD inserter, and the process repeated one month later. There were only 8 18 pregnancies among the more than 3 1,000 women, no deaths, and only 8 serious complications. Comparable figures for surgical tubal ligation would be 30 deaths and 1000 or more serious complications. Comparable figures for no sterilization (and therefore childbearing), leads to estimates of 242 maternal deaths among this many patients. The procedure is thus life-saving, simple, and relatively effective, - at a cost of less than \$1 for both insertions.

An article in the British medical journal Lancet described the Vietnamese clinical trial (1993; 342: 213-217), concluding that the quinacrine procedure held high promise for the country and its needs, given the low cost, ease of application and high success rate.

Within two months of the publication of the Lancet article, a response critical of the Vietnamese field trials was circulated privately. It was authored by the medical director of AVSC, the Association of Voluntary Surgical Contraception: the very folks who have the most to lose if chemical sterilization displaces surgical ligation. Then, an officer of the UN's World Health Organization (WHO) raised the specter of quinacrine causing cancer, -

despite the fact that so far no cancer has been found in any of the follow-up studies (even among Chilean patients of two decades ago), none was reported after wide use of the drug during WW II, and extrapolating from bacterial *in vitro* studies is bad science. However, the well-known Catholic influence within WHO has made the organization historically resistant to family planning initiatives.

Instead of writing their criticisms to Lancet and letting the original authors answer, these oppositional groups spoke only in private venues and refused to respond openly to requests both from Lancet and from the Vietnamese medical establishment. Yet their accusations, although so far unsubstantiated, have brought the Vietnamese trials to a standstill.

From the standpoint of Vietnamese women, quinacrine has been shown to be safer than surgical sterilization, safer than childbirth. The "failure rate" of the procedure might worry women in more developed nations, but it is of less concern when the risks of alternatives are so much higher. There are always legitimate questions about safety, informed consent and efficacy when a familiar drug is used in new ways; the way to answer those questions is to refine the protocol, to build in safeguards, to follow leads in larger clinical trials. But here, the roadblocks appear to be of suspect motivation.

And while women in developing countries search for ways to control family size, theoretical arguments drone on.

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