

WALKING UP DOGS

Q I've read about a new treatment for endometriosis using a GnRH agonist. Can you tell me more about it?

A The optimal treatment of endometriosis remains elusive. In general terms, there are two main types of treatment, surgical and medical. While the idea of surgically removing these abnormally located implants of uterine lining is appealing, surgery is not always the best or most desired form of treatment. On the medical side, danazol (Danocrine), a synthetic drug derived from testosterone, has been the most commonly used treatment, but it also has many side effects. In an effort to find a more satisfactory non-surgical therapy, physician investigators have been actively studying a new class of drugs called gonadotropin releasing hormone (GnRH) agonists. These synthetic drugs cause marked but reversible suppression of the pituitary hormones, FSH and LH. Without FSH and LH to stimulate the ovary, ovulation and the production of the ovarian hormones, estrogen and progesterone, stop. Without estrogen as a stimulus the endometriosis stops growing, and the body's immune system has a better opportunity to destroy it.

There are also side effects associated with GnRH agonists, namely hot flashes. The medication induces a pseudo-menopause. Other side effects which are far less common include headaches, weight gain, decreased breast size, decreased libido and mood changes. These all disappear once the medica-

tion is discontinued. The main problem, however, seems to be a loss of bone density which occurs in women with estrogen deficiency. Bone density is not a problem with danazol because its testosterone-like activity actually stimulates bone formation. After six months of GnRH agonist therapy, bone density has been shown to decrease by 10%. This density will be regained, however, six to twelve months after discontinuing the medication.

The only GnRH agonist currently available is leuprolide (Lupron). This drug is presently approved only for use in males with prostatic cancer. (In males it lowers testosterone levels.) It is given as a daily subcutaneous injection (just beneath the skin), and one month's supply costs between \$135 to \$270, depending on the dose used. A newer agonist is nafarelin which is administered as a nasal spray. This drug has undergone several years of clinical trials and appears well on its way to FDA approval for the treatment of endometriosis. Further studies will be required, however, to prove that the bone density loss is completely reversible. It's hoped that these studies will be completed and the drug will be available within the next two to three years.

So, how effective are GnRH agonists? Studies with nafarelin—and other agonists are likely to be comparable—have shown that it is at least as effective as danazol in treating the symptoms of endometriosis and infertility. Patient acceptance of the drug is higher because of fewer side effects. The medication can be used by itself or in conjunction with surgery, either before or after. Current research with

nafarelin is focused on whether a short, three month course of treatment will yield the same improvement as that found in the six month studies. The obvious advantages of the shorter course are less time away from attempting pregnancy, less expense, and less effect on bone density. Furthermore, women with more extensive endometriosis might be able to take short, intermittent courses of nafarelin to avoid surgery.

At this time, it looks like GnRH agonists offer an exciting new approach to the management of endometriosis. Again, leuprolide is the only agonist currently marketed, and it is an approved drug for an unapproved indication. Your doctors can use it if they feel it is in your best interest. The major advantage of nafarelin is that it is administered as a nasal spray, a much more acceptable delivery system; but nafarelin is currently available only through physicians participating in these clinical trials. You can ask your doctors if they are involved or know of a physician who is. If you participate in a drug study, the drug may be free. Hopefully, nafarelin will soon be available to all patients, as I believe it is a very useful new drug for the treatment of endometriosis. ■

by G. David Adamson, M.D.

Dr. Adamson is Director of The Fertility and Reproductive Health Institute of Northern California and Clinical Assistant Professor, Stanford University Medical Center, Palo Alto, California. He is also a physician investigator for the nafarelin clinical trials and has published several articles on these studies.

