Know When To Treat, When to Refer for infertility

Patient age is perhaps the most important factor in choosing whether to go with treatment or referral.

By BETSY BATES  Los Angeles Bureau

San Francisco — Many young in fertile decades can be worked up and started on a course of therapy without referral to a reproductive endocrinologist or fertility clinic, said Dr. Charles E. Miller at Perspectives in Infertility, said the Naperville, Ill., fertility specialist and family physicians play a critical role in educating patients and their partners about infertility, as well as men with severe semen deficiencies, including problems with sperm morphology.

In remaining couples, a simple work up can be done, but it should be done correctly, preventing the need for repeat examinations. For example, a day 3 follicle-stimulating hormone (FSH) level below 10 mIU/L is an important marker of impaired ovarian reserve, but it should not be interpreted in isolation, said Dr. Miller. Estrogen counts, too.

“If I see an FSH of 8 and an estradiol of 90, that looks every bit as normal to me as an FSH of 15 and an estradiol of 50,” he said.

The age of the patient also provides context with regard to her FSH levels, which can fluctuate. Low FSH rates are less of a concern in the reproductive years, but it should not be interpreted in isolation. Impact infertility tests and procedures that may be performed by general ob gyn and family physicians.

► Laboratory tests. For day 3 of a woman’s cycle, Dr. Miller orders an FSH, estrogen, luteinizing hormone (LH), thyroid-stimulating hormone (TSH), fasting prolactin.

► Ultrasound. Obtain a baseline ultrasound to sound the follicles on day 3 of the cycle to assess the presence of small “resting” antral follicles less than 9 mm in each ovary. Fewer than six total antral follicles (in both ovaries) is a predictor of poor outcome; these patients should be referred. Then have the patient start a urine ovulation predictor kit at midcycle (day 11 if the patient has a 28-day cycle, but day 13 if her cycle is 30 days). Immediately following a positive color change, have the patient connect for another ultrasound. Assess follicle production. A mature follicle that contains a mature egg should be 15-20 mm. Look again at the patient’s estradiol, since a mature follicle may produce a serum estrogen of 200 pg/mL. If no follicle is 15-20 mm, continue monitoring until you get a follicle at least 15-20 mm. If there is no follicle at 22 mm, consider with caution periovulatory levels. Time it based on cycle length.

► Postcoital test. Aspirate mucus from the surface of the cervix 2-6 hours after the couple has had intercourse at midcycle. A normal result is seen just as in the ovulation predictor test. Primary care physicians still use this as a general screen to evaluate the viscosity of the mucus and the acrosomal reaction. If there is no sperm, the test is normal. The patient should be referred if either is abnormal. This test is generally not used by reproductive endocrinologists, who move directly on to treatment if there is an indication of sperm dysfunction.

► Hysterosalpingogram. Schedule the test for day 6-12 to assess the structure and patency of the fallopian tubes.

► Midluteal progesterone levels. Timing is everything with this test, said Dr. Miller. “I see clinic after clinic after clinic... getting a day 21 progesterone [in a patient with an anovulatory cycle] and say, ‘Well, I don’t get that progesterone level a week after ovulation and a week prior to menstruation. Time it based on cycle length.”

► Clomiphene challenge test. Draw a day 3 FSH and estradiol, and order clomiphene citrate, 100 mg daily on days 5-9. Draw FSH again on day 10. A poor prognosis is associated with either an abnormal day 3 FSH or day 10 FSH, or if the sum of the day 3 and day 10 FSH is less than 26.

► Surgery. Consider with caution performing minimally invasive procedures to correct anatomic problems, scarring, adhesions, endometriosis, or fibroids, although the cost of surgery and the potential advantages of in vitro fertilization should be considered.

► Fertility drugs with surgery. If the woman’s follicles do not develop to a mature size or her estrogen or progesterone levels are low. Dr. Miller considers several courses of clomiphene citrate at low doses (50 mg for 5 days on days 3-7 or days 5-9.) Ovulation will occur in 80-85% of women, and over four cycles, 40% of women will become pregnant.

However, pregnancy rates are much lower in older patients.

“I can tell you that[40% pregnancy rate] does not happen in my 38-year-olds. I do not use this medication in women over 40. I feel that we are just wasting time.”

However, in well-selected young patients, the strategy is worth a try, since it is inexpensive, easy, and not associated with an unacceptable rate of multiple births.

“For a generalist, this is a safe drug to use for 3-4 cycles, particularly in younger patients. Then move that patient on,” Dr. Miller said.

Patient Trust Is the Key to Getting Infertility Facts Across

By BETSY BATES  Los Angeles Bureau

San Francisco — Ob.gyns. and family physicians play a critical role in educating patients and their partners about infertility, doing a basic work up, and knowing when to refer them without delay to a specialist, according to Dr. Charles Miller.

Receiving factual information from a trusted source will go far in combatting deeply entrenched myths and misconceptions about infertility, said the Naperville, Ill., infertility specialist and family physician during Perspectives in Women’s Health sponsored by OB.GYN. News.

“We are not reaching them,” he said. “Despite Redbook and Oprah and Marie Claire... Time magazine, Newsweek, and U.S. News and World Report, we’re just not getting there.”

Dr. Miller said he was “shocked” to learn from a recent national survey sponsored by the National Infertility Association RESOLVE that the majority of women could not define infertility and had heard of the No. 1 cause of the problem was stress.

Among the facts women need to know:

► Infertility is defined as failure of a woman 35 or younger to become pregnant in 1 year, or in 6 months if the woman is over 35.

► Fecundity rates decline quite precipitously after the first six cycles of attempting to achieve pregnancy.

► There are 7.7 million couples experiencing infertility in the United States today.

► One in three U.S. couples aged 35-39 years will not be able to achieve pregnancy without treatment.

► The risk of Down syndrome and other chromosomal abnormalities increases sharply as women age: estimated to be 1 in 11 live births and 1 in 8 live births, according to Dr. Miller, when the sperm in a woman who delivers live at age 49.

► The live birth rate for in vitro fertilization in women over the age of 40 is approximately 10-15% at most centers.

Dr. Miller pointed out that the age-related decline in fertility has been documented since the 17th century “This is nothing new. This is not because of STDs, not because of more fibroids, not because of the cause of diet. This is because of egg production.”

Most of the causes of infertility are physical, not psychological, he said.

Among female factors, ovulatory factors are responsible for infertility in about 15% of cases, uterine and tubal factors combine to contribute to about 40% of cases, and endocrine factors are responsible for about 15%.

Varicoceles are much more common in men than women, but the difference is more apparent in other causes of infertility, said Dr. Miller. “I see clinic after clinic after clinic... getting a day 21 progesterone [in a patient with an anovulatory cycle] and say, ‘Well, I don’t get that progesterone level a week after ovulation and a week prior to menstruation. Time it based on cycle length.”

He said he believes antiangiogenic antibodies probably do not help fertility, but the role of other antiphospholipid antibodies is less clear.

“No there are physicians who will work this up to the hilt, and there are groups of physicians who will ignore it,” he said.