

Treat Some Tubal Disease Prior to ART

BY BETSY BATES
Los Angeles Bureau

PASADENA, CALIF. — The conundrum of whether tubal disease should be treated before moving on to assisted reproductive technologies has persisted for nearly 3 decades—since in vitro fertilization was first developed to compensate for tubal dysfunction.

During a recent talk at the annual meeting of the Obstetrical and Gynecological Assembly of Southern California, Dr. Michael P. Diamond, director of reproductive endocrinology and infertility at Detroit Medical Center and Wayne State University in Michigan, offered his recommendations concerning the following three forms of tuboperitoneal disease:

Endometriosis

A number of relatively small studies and a metaanalysis suggest that significant diminishment of success rates for assisted reproductive technologies seems to occur mostly in women with stage III or IV endometriosis and particularly in those with large endometriomas, but not so much in women with less severe endometrial disease.

Early studies pointing to impaired pregnancy outcomes may be reflective of difficulties in laparoscopic oocyte retrieval, rather than success of the assisted reproductive technologies (ART) process itself. Dr. Diamond therefore recommends prior treatment of late-stage endometriosis with GnRH analog and possibly surgery when



there is hope of reducing endometriomas, improving the environment for ART, and reducing toxicity associated with extensive endometriosis. The jury is still out with regard to treating stage I-II endometriosis before moving forward with ART, he said.

Hydrosalpinges

Hydrosalpinx has the potential of reducing fertility via a number of mechanisms, including deprivation of embryos of nutrients in the endometrial cavity and embryonic toxicity associated with exposure to hydrosalpinx fluid.

Hydrosalpinx can also impair endometrial receptivity through altered integrin expression, interleukins, progesterone receptors, and other factors.

It may interfere with normal endometrial peristalsis, and finally, in “a very mechanistic process,” it can cause embryos to literally wash out of the fallopian tube.

A Cochrane Database review shows that pregnancy and live birth rates were significantly improved if salpingectomy was performed prior to ART for patients with true hydrosalpinges (Cochrane Database Syst. Rev. 3:CD002125, 2001, update 2004).

However, “that’s not the whole story. That’s not how all of these patients present,” he said. There is no evidence in the literature that surgery improves ART outcomes for patients with mild tubal disease.

It is also unclear what the best course of treatment is for patients who have no evidence of hydrosalpinges on ultrasound,

but who develop filling of the tube during a diagnostic hysterosalpingogram.

Pelvic Adhesions

If a patient is going to undergo ART for infertility, will adhesions around her ovaries and fallopian tubes have any deleterious effect on the procedure?

In fact, there have been papers that suggest that is the case, he said. Japanese researchers have demonstrated that periovarian adhesions interfere with diffusion of gonadotropins into the follicular fluid during IVF treatment, affecting both the follicular human chorionic gonadotropin (hCG) concentration and the ratio between follicular hCG and serum hCG concentration (Hum. Reprod. 1998;13:2072-6).

Very early studies by Dr. Diamond and associates were able to document the presence of adhesions over time when oocyte retrieval was achieved through laparoscopy (Fertil. Steril. 1988;49:100-3).

These studies found that although the number of follicles was not affected by periovarian adhesions, the number of oocytes retrieved was reduced by about a third, he said. The bottom line is that oocytes can still be obtained in patients with periovarian adhesions, and surgery offers no assurance of cure. Indeed, several studies suggest more extensive adhesion formation following surgery.

“While the data are mixed, I think there is good evidence you can get very reasonable ovarian response to gonadotropin stimulation even in the presence of pelvic adhesions and even if they’re extensive around the ovary,” he said adding that surgery for adhesions “probably would not justify the expense and morbidity of a surgical procedure.” ■

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DR. DIAMOND

Puberty Now Hits Many Girls Before Menarche

BY DEEANNA FRANKLIN
Associate Editor

Unlike girls born at the turn of the last century, young girls today increasingly show minimal correlation between onset of puberty and age at menarche, reported Dr. Frank Biro and his colleagues.

In their study, 541 black girls and 615 white girls, all aged 9 years, were given annual exams over 10 years. At the start, 49% of the black girls and 77% of the white girls were prepubertal.

The participants, born in 1977 and 1978 and socioeconomically diverse, were recruited from public and parochial schools in Cincinnati, Richmond (Calif.), and an HMO in Washington (J. Pediatr. 2006;148:234-40).

The onset of puberty was defined as “the age at areolar stage 2 or at pubic hair stage 2, whichever occurred earlier. Age of menarche was calculated from the date of birth to date of first menstrual period,” said Dr. Biro of Cincinnati Children’s Hospital Medical Center, and his colleagues.

At the end of the study only a moderate correlation was found between onset of puberty and age of menarche. The median age for onset of puberty for white

girls was 10.2 years and a mean age at menarche was 12.6 years; for black girls, it was 9.6 years for onset of puberty and 12 years for age at menarche.

Participants completed puberty at a median age of 14.3 years for whites vs. 13.6 years for blacks. Blacks also had a significantly younger age for several other puberty parameters such as age at peak height velocity (11.5 years vs. 11.9 years for whites), end of puberty, defined as attainment of areolar 4/pubic hair 5 (13.6 years vs. 14.3 years for whites), and age at attainment of adult height (16.5 years vs. 17.1 years for whites).

The median interval between age at onset of puberty and start of menarche was 2.7 years for blacks and 2.5 years for whites.

Researchers contrasted their results to several earlier studies including a 1948 study by Dr. E. Reynolds and Dr. J. Wines that showed a very close correlation between onset of puberty and age of menarche for girls born during the 1930s (Am. J. Dis. Child. 1948;75:329-50). However, the 1999 Bogalusa Heart Study found that the median age of menarche had dropped by almost 10 months in blacks vs. 2 months in whites for the period between 1973 and 1994 (Ethn. Dis. 1999;9:181-9).

According to Dr. Biro and his colleagues, the age of onset of puberty may be influenced by interplay “between genes and the environment.” The reasons for this “temporal drift” in the correlation results may “reflect interactions between body composition, environmental influences (such as endocrine disruptors) and genetic polymorphisms.”

They took into account the possible role that fat, particularly leptin, might play in this decreasing correlation. Girls with earlier menarche tended to have higher BMIs, and “leptin appears to serve a permissive factor for the onset of puberty. Leptin levels are greater in blacks, even with adjustment for fat mass and pubertal maturation.” However, “the increases in relative weight ... may be a consequence rather than a determinant of age of menarche, or secular changes in BMI and mean age at menarche could be independent phenomena,” the investigators said.

Dr. Paul Kaplowitz, a pediatric endocrinologist at Children’s National Medical Center, Washington, was not surprised by the study’s results. “It confirms what many of us have seen [that] there is a lot of variability in how rapidly different girls progress through puberty.” ■

Warn Teens of Promiscuity’s Fertility Risks

BY SHERRY BOSCHERT
San Francisco Bureau

KAILUA KONA, HAWAII — Think of both ends of the fertility spectrum when advising women about preventing or treating cervical cancer, Kimberly D. Baker, J.D., said at a conference on obstetrics, gynecology, perinatal medicine, neonatology, and the law.

An increasing number of malpractice cases are being brought by teenagers who claim that no one adequately explained the risks of sexual activity and of avoiding Pap smears, said Ms. Baker, a defense lawyer in Seattle who also holds a bachelor’s degree in nursing.

These adolescents lack an understanding of the threats that sexual activity and a lack of screening can pose to their bodies, their fertility, and even their lives if they contract a sexually transmitted disease. Physicians “are being too casual about this,” she said. “You need to document exactly what you said” in counseling the patient.

Explain things in terms that the teenager can understand, Ms. Baker said at the conference, which was sponsored by Boston University.

If a cervical lesion needs treatment, be sure to discuss the potential effects on fertility—especially when counseling young patients and older patients, she added. As more and more women delay childbearing, an increase in malpractice cases related to cervical cancer is being seen on the older end of the premenopausal age spectrum when treatment fails to protect fertility and the patient isn’t warned of possible effects on fertility.

“Along with that, there needs to be a frank discussion about what is not available to them” if cervical cancer treatment affects fertility, she said. Without that discussion, women who cannot get pregnant may waste time, money, and energy on assisted reproductive technology that may not be appropriate for them.

If your “bedside manner” isn’t the best, consider putting patients with cervical lesions in touch with a mental health care provider to provide support. Lack of rapport between patients and providers is a major contributor to lawsuits, Ms. Baker said.

Obstetricians need to keep in mind the whole health of the patient, not just the pregnancy, she added. In one case, a 22-year-old woman had Pap smears taken just before a pregnancy and in the first postpartum exam, but neither was followed up. She died of cervical cancer 18 months after giving birth to the child.

“While you’re trying to be excited about the birth of her child and talking about contraception, weight loss, or whatever, be mindful” of conducting Pap smears and following up on results, she advised. ■