

## The right tests may unlock mystery of miscarriage

**P**ATIENTS ARE BECOMING more proactive, in part because they have access to more resources than ever before. But when it comes to miscarriage—particularly ones that occur before 10 weeks—they're often left without answers.

With the expanding use of ultrasound monitoring for ovulation induction and in vitro fertilization, more women are now aware of preclinical miscarriages prior to six weeks of gestation. In addition, with the use of over-the-counter, highly sensitive pregnancy tests, miscarriages are being diagnosed even before a menses is missed.

These factors are contributing to a rise in patients seeking evaluation and management of recurrent early pregnancy loss, which refers to two or three or more consecutive pregnancies that end in demise before 15 weeks' gestation.

Why do early miscarriages occur? According to Fellow Mary D. Stephenson, MD, MSc, professor of ob-gyn and director of the University of Chicago Recurrent Pregnancy Loss Program, testing miscarriage tissue for chromosomal abnormalities often provides the answer, yet many times this testing isn't done.

"For decades, we've been evaluating the woman and her partner for recurrent pregnancy loss, but ignoring the miscarriage itself," Dr. Stephenson said. "The first step should be examining the miscarriage tissue for random chromosome errors."

ACOG's Practice Bulletin on the topic acknowledges that many experts obtain a karyotype of the tissue but states that definite recommendations for routinely obtaining tissue karyotypes cannot be made (Practice Bulletin #24, *Management of Recurrent Early Pregnancy Loss*, February 2001, reaffirmed 2008).

Research shows that in miscarriages that occur prior to six weeks' gestation, 70% of the time it is due to numeric chromosome errors, such as trisomy, monosomy, or polyploidy. This information can help patients, but if testing does not occur, questions remain, accord-

ing to Dr. Stephenson. Miscarriages that occur between six and 10 weeks are associated with chromosome errors 50% of the time; after 10 weeks, it drops to 5%, she said.

It is not necessary to have a D&C to collect miscarriage tissue: the patient can collect her own at home. With D&C, chromosome results are obtainable 90% of the time; with expectant management, 66% of the time (Stephenson et al, *Human Reproduction*, 2002;17:446-451). When performing a D&C, physicians must isolate the pregnancy tissue from the specimen.

"Commonly, both maternal decidua and miscarriage tissue are tested. Then we get a 'normal female' result back, which is often incorrect," Dr. Stephenson said. "The pregnancy tissue must be separated and cleaned."

If a "normal female" result occurs, another step can be taken: the DNA in the patient's blood can be compared to the miscarriage DNA. If the DNA fingerprinting is different, then maternal cell contamination has been excluded, meaning the "normal female" result is correct.

### Thrombophilias not sole answer

Like Dr. Stephenson, Fellow William H. Kutteh, MD, PhD, director of Fertility Associates of Memphis and ob-gyn professor and director of reproductive endocrinology at the University of Tennessee, is committed to determining causes of recurrent early pregnancy loss.

Dr. Kutteh believes it is particularly important not to lose sight of established diagnostic and treatment strategies. Recently, he has noticed that thrombophilia testing is happening too soon and too often.

"I compare the current focus on thrombophilias to what happened 14 years ago when antiphospholipid antibody syndrome was recognized as a cause of RPL," he said. "Many thought it was the cause of all RPLs, and they began to overlook a careful evaluation of the uterus. Today, thrombophilia panels are often ordered before completing basic evaluations."

### WORDS CARRY WEIGHT

Reproductive endocrinology experts Drs. Mary D. Stephenson and William H. Kutteh believe that terminology such as "habitual abortion" used to describe early recurrent pregnancy loss must be eliminated because it suggests there was a choice to terminate the pregnancy. They say this includes changing ICD-9 terminology from "habitual aborter, non pregnant" to "recurrent pregnancy loss" and eliminating all informal or oral usage of this language.

According to Dr. Kutteh, basic evaluations include:

- ▶ **Genetic:** karyotypes on both partners
- ▶ **Anatomic:** evaluation of the uterus by sonohysterography, hysterosalpingography, or hysteroscopy
- ▶ **Endocrine:** Some experts, including Dr. Kutteh, advise testing thyroid-stimulating hormone levels in women with recurrent pregnancy loss. ACOG's Practice Bulletin states that such tests are not required in otherwise normal women with RPL and no treatments have proven beneficial in women with antithyroid antibodies
- ▶ **Immune:** tests for lupus anticoagulant and anticardiolipin antibodies, both IgG and IgM
- ▶ **Thrombophilic:** Recent metaanalyses indicate that factor V Leiden and factor II (prothrombin) are important risk factors

Evaluations can be completed by general ob-gyns with up-to-date knowledge of immunology and thrombophilias, Dr. Kutteh said. Otherwise, the couple should be referred to a specialist. ♀

### info

→ ACOG Practice Bulletin *Management of Recurrent Early Pregnancy Loss* (#24, February 2001, reaffirmed 2008): [www.acog.org/publications/educational\\_bulletins/pb024.cfm](http://www.acog.org/publications/educational_bulletins/pb024.cfm)