Boston — Estrogen-containing oral contraceptives appear to greatly increase the relative risk of venous thromboembolism among women with the factor V Leiden genetic mutation, according to a recent review by the World Health Organization.

Asked if they would prescribe estrogen-containing oral contraceptives for these women, members of a recent expert panel agreed they would not. The risks of a blood clot are too great, they said.

“I’d be very cautious about using estrogen. I would use methods that had progesterin in them if the patient wanted a hormonal method at all,” said panelist Sharon Schnare of the South Kitsap Family Care Clinic in Port Orchard, Wash.

“They really should not use a contraceptive method that has estrogen in it,” agreed Dr. Michael Policar, medical director of the California state office of family planning.

The clinicians spoke during a conference on contraceptive technology sponsored by Contemporary Forums.

Clots: Relative and Absolute Risks

The evidence on the risks of VTE among women who carry factor V Leiden and who also take combined oral contraceptives (COCs) is murky. The research suffers from a variety of biases and sometimes offers conflicting assessments.

Given the evidence, who should receive screening? And what contraceptive methods should those with the clotting gene use?

The WHO undertook its systematic review to answer some of these questions (Contraception 2006;73:166-78). In its analysis of 16 studies, the WHO authors found the following:

• Factor V Leiden alone increased the risk of VTE among women-of-childbearing age by a range of 30% to 30-fold (OR 1.3 to 30).

• Women with the factor V Leiden mutation who took COCs increased their risk of VTE compared with women with neither risk factor by 6.4 to 99-fold.

• Compared to nonusers with the mutation, women with the mutation who took COCs increased their risk of VTE by a range of 30% to 25-fold (OR 1.3 to 25.1).

• The absolute risk of VTE remains rare; 99.9% of women who carry the mutation would not have thrombosis if they received oral contraceptive pills.

• In one analysis of women carrying the clotting gene, first- and second-generation COCs were more than twice as likely to be associated with a VTE (OR 64.7) as were third-generation pills (OR 29.6).

Despite numerous limitations inherent in the studies they analyzed—and the tremendous variation in how studies were conducted—both the WHO authors say it is possible to tease out at least one definitive conclusion. “The data overwhelmingly suggest that COCs is a risk factor for VTE,” the authors write.