

# Combo OC Use in Factor V Leiden Not Advised

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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 progestin 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 child-bearing age by a range of 30% to 30-fold (OR 1.3 to 30.0).

► 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 variability in the studies' results—the WHO authors say it is possible to tease out at least one definitive conclusion. "The data overwhelmingly suggest that there is a multiplicative effect at work—the combination of factors produces greater risk than thrombogenic mutation alone," they write.

## Screening, Contraceptive Advice

The WHO does not recommend routine screening for thrombogenic mutations. The yield would be tiny, the number of lives saved minuscule, and the cost astronomical. According to one cost-effectiveness analysis, clinicians would have to screen 92,000 factor V Leiden carriers at a cost of nearly \$300 million to prevent one death from VTE attributed to COCs (*Fertil. Steril.* 1999;72:646-51).

Unfortunately, no one has looked at risks

associated with other forms of contraception among women with thrombogenic mutations, according to the WHO authors. On the basis of two reports—a postmarketing surveillance study of Norplant (*Contraception* 2001;63:187-209) and an international, multicenter, case-control study conducted by the WHO (*Contraception* 1998;57:315-24)—they conclude that there is "limited evidence" that progestin-only methods and combined injectable contraceptives do not increase the risk of VTE.

Doing nothing is perilous in a woman of childbearing age carrying the factor V Leiden mutation because pregnancy is also a risk factor for VTE in these women, Dr. Policar told the audience. "While an estrogen-containing contraceptive is dangerous, pregnancy is also really dangerous," he noted. "If a patient reveals to you that she has factor V Leiden and she is not actively trying to get pregnant right now, it's extremely important that you help her obtain effective contraception," he said. ■

## Vitamin D—both its importance and the amount needed—cannot be underestimated for proper calcium absorption AND OPTIMAL BONE HEALTH

### How much proof is there that vitamin D is essential to bone health?

Volumes.

#### Vitamin D is critical

To help maintain normal blood levels of calcium and absorb the calcium needed to form and help maintain strong bones, vitamin D is essential.<sup>1</sup> Most calcium absorption occurs in the small intestine.<sup>2</sup> Without vitamin D, the small intestine absorbs only a fraction of dietary calcium. In a study by Heaney et al, vitamin D increased calcium absorption by as much as 65%.<sup>3</sup>

#### Vitamin D insufficiency is becoming an epidemic problem, especially for older Americans<sup>4,5</sup>

The majority of Americans do not achieve adequate vitamin D levels.<sup>6,7</sup> 90% of older adults aged 51 to 70 (and 98% of those over 70) are not getting adequate vitamin D from their diet.<sup>6,7</sup> But inadequate intake isn't limited to just postmenopausal women and the elderly. More than two thirds of adolescent and adult women do not meet the adequate intake of vitamin D from their diet.<sup>6,7</sup> Clearly, something needs to be done.

#### "...[current] recommendations are totally inadequate..."<sup>4</sup>

Current recommendations for daily vitamin D intake were established almost a decade ago. Many experts now agree that the daily recommended intake is too low.<sup>4,8-12</sup> The response to vitamin D supplementation in clinical trials is further evidence that patients can benefit from higher levels of vitamin D. Emerging research suggests that getting at least 750-800 IU of vitamin D daily is associated with improved bone and muscle health in the elderly.<sup>8,13</sup> Furthermore, a meta-analysis by Papadimitropoulos et al suggests, "Vitamin D decreases vertebral fractures and may decrease nonvertebral fractures."<sup>13</sup> Zittermann states, "Current estimations for an adequate oral intake are obviously much too low to achieve an optimal vitamin D status..."<sup>10</sup>

Many experts agree: *the lowest daily dietary intake for vitamin D for adults should be at least 750-800 IU per day.*<sup>4,8,11,12</sup>

#### Why Rx osteoporosis therapy still requires calcium and vitamin D

Rx treatments, including bisphosphonates, uniformly require sufficient calcium intake. However, as the use of these drugs has risen, a simultaneous decrease in the use of calcium supplements has occurred.<sup>14</sup> This may be a result of patients believing that their Rx drug replaces their need for calcium. In addition, the majority of this population fails to consume the minimum recommended dietary intake of calcium, making calcium supplementation more critical.

Adequate vitamin D intake must also be taken into consideration.<sup>15</sup> As noted in FDA's official magazine, for those receiving osteoporosis treatments, calcium and vitamin D supplements can be essential.<sup>16</sup> Yet, more than half of North American women receiving therapy to treat or prevent osteoporosis have inadequate levels of vitamin D.<sup>17</sup> This population needs to understand the importance of getting the right amount of calcium and vitamin D every day.

#### When patients need more D, you need to recommend a supplement

Very few foods are natural sources of vitamin D. And while sunlight is an excellent source of vitamin D, many individuals limit sun exposure or use sunscreen, which interferes with vitamin D synthesis of the skin, putting them at increased risk of inadequate vitamin D levels. In addition, as many people age, their ability to produce vitamin D decreases. Calcium supplements with added vitamin D are an excellent way to help ensure patients get the D they need daily for optimal bone health. It's never too soon to improve bone health. And it's never too late. The US Surgeon General states, "...[for those] not getting enough calcium and vitamin D in your diet, supplements can be bone savers."<sup>18</sup>

#### Together, calcium and vitamin D can transform the future of bone health

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