



## EDITORIAL

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# VTE and OCs With Drospirenone— Proceed With Caution

In the past few years, several studies evaluated whether the use of drospirenone-containing oral contraceptives (OCs) increased the risk for deep venous thrombosis (VTE) and pulmonary embolism compared with use of “older” OCs, particularly those containing levonorgestrel. Two recently published studies on the same topic have caught the attention of the lay press, resulting in many patients becoming concerned about and questioning the safety of their OCs.

Although 2 studies published in 2007 failed to show any differences in risk, 4 studies published in the *British Medical Journal*, 2 in 2009 and the 2 most recently in 2011, have suggested that use of drospirenone-containing OCs increases the risk of VTE, compared to the older preparation. Before we can accept any of these results at face value, it is worth examining the problems inherent in conducting such studies.

All the studies that have examined the OC issue are observational, as the risk of VTE in young women, even those with risk factors, is low. Although randomized clinical trials are considered scientifically preferable—since randomization, if successful, reduces confounding—the cost in both time and money to evaluate the risk for a rare condition such as VTE in the reproductive age-group is quite prohibitive.

Both cohort and case-control

studies are subject to more confounding than a randomized trial, since the investigators have no control over who gets exposed to what drug. Well-known factors such as age can be controlled in many studies; however, in the case of VTE, other factors such as presence of a thrombophilia or another condition that affects VTE risk may not

In a recent opinion article, Grimes noted an inaccuracy rate of almost 60% when chart review of this diagnosis was carried out within a Danish registry! Among the 6 studies noted in this editorial, half relied upon material that was in the database and did not fully review the original clinical records. Of note, the Seeger study that showed no dif-

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be ascertained and/or may more likely present in one group because of a prescribing preference.

Upon review of the recent 6 studies, some type of registry or database was used in all of the studies to form their cohorts or identify cases and controls. Registries must be able to accurately assess exposure, the outcome measures of interest, and other risk factors that might affect the outcomes, in order to be scientifically useful in studies. Conversely, if there is lack of clarity in any of these assessments, chart review is necessary. In particular, pharmacy or claims databases may fall into this dilemma and be particularly inaccurate in assessing VTE.

ference included a medical record review of the VTE cases. Although assessment of exposure to agents such as OCs is fairly accurate in most claims databases, they do not fully assess other risk factors.

A significant advantage of the Dinger study, which also showed no difference in risk, was that it was designed specifically to prospectively gather information on possible cases of VTE as well as risk factors. Although problems such as accuracy of ascertainment, as well as issues with various study designs, have led to lack of clarity, we cannot assume that differences among OCs relative to VTE do not exist.

So what do we tell our patients

when they ask about this issue?

First, we can tell them that the results have been inconsistent and if there is a risk, it is difficult to assess the magnitude because of the problems inherent in studying this condition. Secondly, the risk of VTE associated with any OC use is still substantially smaller than the risk of VTE in pregnancy. Further,

to date, the FDA has not restricted or halted the sale of any of these OCs nor has it required any substantial change in labeling.

Finally, as a practitioner, it is important to note that the CDC/WHO "U.S. Medical Eligibility Criteria for Contraceptive Use, 2010" document assumes relative to VTE risk that all types of low-dose

estrogen-containing contraceptives, regardless of their progestin content, are similar in risk relative to VTE; ie, it is a class effect.



**Ronald T. Burkman, MD**  
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**SUGGESTED READING**

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