

**Journal Club Synopsis**  
**From July 12, 2012**

**Discussion Leader: Susan Geiger MD**  
**Host: James Olson Ph.D.**

**"In the pregnant patient with shortness of breath, chest discomfort, and leg edema, is the d-dimer test sensitive to rule out pulmonary embolism"?**

**Clinical Scenario:**

You are working A Pod at Kettering and a 29 yo G1 at 32 weeks has just checked in to triage. On interview and exam she also reports some possible unilateral leg edema yesterday, though there is none present on exam. She does report some chest pain, but she thinks it's "just reflux". You are concerned about possible PE but you'd hate to expose her growing creature to any unnecessary radiation.

You've heard a few attendings talking about using the d-dimer test on pregnant patients with new ranges based on trimester, and are wondering if this is sensitive and specific enough to get your patient out of getting a CT scan while pregnant.

**Introduction:** Though there is still some question over exactly which imaging exam is appropriate for a pregnant person with possible PE, at this time we are still focusing on using CT of the chest for this population. There is an obvious risk associated with this and avoiding it is preferable. Recently there have been several attempts at quantifying the physiologic range of the d-dimer value in pregnant individuals in hopes that we can utilize d-dimer for this population as we do in otherwise low-risk, non-pregnant patients.

**Article 1:**

Evaluation of D-dimer during pregnancy. Nishii A, Noda Y, Nemoto R, Ushiro K, Ohno T, Mochizuki Y, Yoshihara H, Taguchi A, Uchino N, Ohkawara S. *J Obstet Gynaecol Res.* 2009.

This study out of Japan focused on testing d-dimers of women in the first and third trimesters of pregnancy to elucidate new "normals" for this population. Additionally DVT screens were performed by ultrasound during the third trimester to correlate a certain d-dimer number or range to those women who ended up with positive scans. D-dimers were found to be elevated over the typical, non-pregnant baseline –  $1.1 \pm 1 \mu\text{g/ml}$  in the first trimester and  $2.2 \pm 1.1 \mu\text{g/ml}$  in the third trimester. The study did indicate a statistically significant increase in the d-dimer of those with positive DVT screens in the third trimester, this number was found to be  $2.6 \pm 1.2 \mu\text{g/ml}$ . Therefore they elected to take  $3.2 \mu\text{g/ml}$  as the threshold for likely presence of DVTs.

**Group Discussion:** The group's bottom line was that while this article did delineate the truth that d-dimers rise in pregnancy, it did not prove that there are specific numbers by trimester that can be thought of as "normal" and not representative of a possible DVT. Additionally, the article's discussion of d-dimer in relation to the number of gestations (twin vs singleton) as well as BMI furthered our impression that the research had not provided the concrete numbers the authors had hoped for and this additional information was seemingly added as a second thought.

### **Article 2:**

The use of D-dimer with new cutoff can be useful in diagnosis of venous thromboembolism in pregnancy. Kovac M, Mikovic Z, Rakicevic L, Srzentic S, Mandic V, Djordjevic V, Radojkovic D, Elezovic I. *Eur J Obstet Gynecol Reprod Biol.* 2010 Jan; 148(1):27–30.

The goal here was to establish new “normal” ranges for each trimester. This was done by measuring the d-dimer level in 89 pregnant women during each trimester. To examine what level represents a likelihood for DVT, d-dimer levels in 12 women with suspected DVTs were also measured. Results of this study revealed that d-dimer rose predictably throughout each trimester and the authors established 286 as the cutoff for “normal” in the first trimester, 457 for the second and 644 for the third.

**Group Discussion:** While this was the only study we discussed which set out new specific standards for each trimester, we noted that it was a rather small sample group of healthy pregnant women and an alarmingly small group of those with positive DVTs – only 12. Furthermore, despite establishing new cutoffs for d-dimer, this study’s data revealed that there were women in the second trimester with known venous thromboemboli who technically tested “negative” within the new cutoffs. Knowing that our community has a nearly no tolerance attitude for missing DVTs, especially in pregnant women, and there are actually two patients at risk in this study, this conclusion was unacceptable to us. Therefore it was the group’s opinion that these cutoffs were not established over a broad enough study population to utilize at this time.

### **Article 3:**

D-dimer testing in pregnant patients: towards determining the next 'level' in the diagnosis of deep vein thrombosis. Chan WS, Lee A, Spencer FA, Chunilal S, Crowther M, Wu W, Johnston M, Rodger M, Ginsberg JS. *J Thromb Haemost.* 2010 May;8(5):1004–11. Epub 2010 Jan 30. PubMed PMID: 20128870.

The study was performed over many years and utilized multiple forms of d-dimer testing in efforts to establish norms. The population consisted of women who presented with suspected VTE. A d-dimer was tested using two rapid enzyme-linked immunosorbent assays and three latex agglutination assays and US were performed to establish the present or absence of DVT. These patients were then followed up with repeat imaging three months later. The authors utilized ROC curves to determine a new cutoff for healthy pregnant women and stated that using these values d-dimer can be used to be both sensitive as well as specific.

**Group Discussion:** This study took the time to test five different methods of testing a d-dimer, and was the only study we reviewed which concentrated on both the specificity and sensitivity. Additionally, ROC curves were utilized to further the illustration of results. However, on initial review their cutoff points appear somewhat arbitrary which may possibly misrepresent the tests’ real ability to be both sensitive and specific, and the study group was relatively small with only 249 subjects who were somewhat self-selected as they were recruited from the study based upon presentation with concern for VTE.

Accordingly, the discussion group was not comfortable in blindly accepting this data as universal truth.

**Overall Discussion:** As a group we felt encouraged that focus is being directed at this possibly useful study in pregnant women. But we quickly recognized, especially in the arena of pregnant patients where emotions and fear may often run high, we were not yet ready to adopt any of these new ranges as fact and base clinical decisions upon them. Additionally, while the populations studied were small, the numbers are against us in general for study on this topic. Fortunately few women end up with a DVT during pregnancy, making the validation of these ranges even more difficult. Additionally, we were really hoping to answer questions about patients with possible pulmonary embolism, and none of these studies mentioned women with symptoms of shortness of breath or pleuritic chest pain. Ultimately it was decided that if our suspicion was raised for PE, a CT scan with appropriate shielding would be performed. And if ruling out DVT was our goal, lower extremity ultrasounds would be ordered. We continue to remain hopeful for additional research in this area.