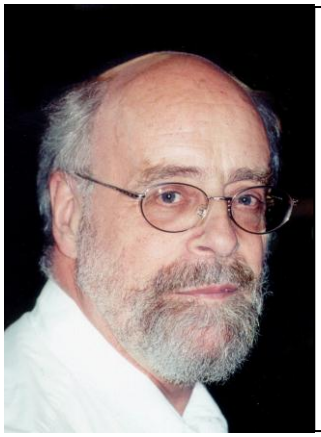
Clinical Chemistry

Whole-Blood Thrombin Generation Monitored with a Calibrated Automated Thrombogram-Based Assay



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Guest:
Professor Coen Hemker is emeritus professor of biochemistry, at the medical facilities of Maastricht, Leiden, & Paris, and Director of Synapse, a research and development company.

Bob Barrett: This is the podcast from *Clinical Chemistry*. I am Bob Barrett. The generation of thrombin is an important step in the clotting cascade and the thrombin generation assay is increasingly recognized as a useful diagnostic tool in the area of thrombosis and Hemostasis.

In the August 2012 issue of *Clinical Chemistry*, French and Dutch researchers described a thrombin generation assay that uses whole blood rather than plasma as a sample. We are joined by one of the authors of that study, Professor Coen Hemker.

Professor, why is it important to measure thrombin generation, rather than clotting times?

Prof. Coen Hemker: Okay, well, because the amount of thrombin that is formed is much more important than at the moment that it starts being formed.

You should know that when blood starts to clot, nothing happens for some time, then at a given moment, it clots, and that is the moment, the thrombin generation begins and after that there is an explosion of thrombin generation and all evidence, up to now, all available evidence shows that the amount of thrombin, the force of the explosion, is much more important medically than just the time that it takes before the explosion start.

And we can even go so far as to say that the clotting time is only important in those cases, which is let's say half of the cases, that it indeed reflects the amount of thrombin that has been formed.

Bob Barrett: And in what sense would that be better?

Prof. Coen Hemker: Because, A) you can now find those people that make too much thrombin. Clotting time cannot become short than normal or hardly. The quick time is 12 seconds and if you

are very, very hypercoagulable, it may be 11.6 seconds, which is not easy to measure and does not give leeway for much variation, whereas the amount of thrombin can be twice as big as normal or one that's half times as big as normal. And when it's twice as big as normal, you are in much more problem than when it's one and a half time as big as normal.

So hypercoagulability can be quantified now. Of course, for every person that dies of bleeding, there are hundreds that die of thrombosis. So hypercoagulability as such is medically much more interesting than hypocoagulability.

Bob Barrett: And just why is it important to detect hypercoagulability?

Prof. Coen Hemker: To find people that are hypercoagulable, for instance, a young girl that is going to take the pill, we will want to know whether she is hypercoagulable and so, has some accrued risk of developing thrombosis.

And also about this, perhaps it's more important, because if you find hypercoagulability, you can do something about it with anticoagulants. And there are many types of anticoagulants, so that each of them require, if they are to become throbs, their own form of clotting time, and they can all be measured as the same type of thrombin generation test.

Bob Barrett: But aren't clotting times so much easier to determine? They seem to be routine in nearly all laboratories?

Prof. Coen Hemker: Oh yes, of course, they are. Well, in the first place they are familiar and then in the second place, they are easy to determine. But the technique of measuring thrombin generation is going very fast and at this moment already it can be measured with throughputs and the accuracy of that is not less than that of any clotting factor determination.

Bob Barrett: But measuring clotting times doesn't require the sophisticated laboratory instrumentation needed for measuring thrombin generation.

Prof. Coen Hemker: Absolutely. Yes. Well, even clotting times are measured with machines these times that are quite sophisticated sometimes, but it's absolutely true that well, if you want to continue with medieval methods, you get medieval information.

Bob Barrett: Well, you do have the human factor that many physicians are not specialists in hemostasis and they'll feel uncomfortable with new laboratory tests.

Prof. Coen Hemker: Oh, that's absolutely true and even worse with coagulation

than with many other things, because there are two types of doctors. Those who like coagulation, that's about 1% and those who hate it and that is 99%. And they hate it for two reasons: A) Because it's very complicated thing, but that as such is not so serious because immunology also is a very complicated thing and so on and so forth.

But the problem is that the basic thing, the uncomplicated thing that a non-specialist wants to know about clotting, are precisely these capricious clotting times, these illogical clotting times. Because not only do they not indicate hypercoagulability, also mild bleeding, this is not detected. Every surgeon knows that mild bleeding tendency that may cause problems during an operation is not excluded by a normal APTT.

Bob Barrett: Well, professor, when will this test be available to clinicians and their patients?

Prof. Coen Hemker: Well, I am a research person and after research and even after development of this, comes a lot of FDI and European Administration before you have the right to apply it to patients.

I am very happy to keep out of that circuit, so I don't know actually, but it is on its way, that is the thing that's certain and for research purposes, it's kind of what's used, well, all over the world, so that's between 700 and 900 laboratories where the method already is available.

Bob Barrett: Well, finally, how would you summarize the relation between thrombin generation and clinical diagnostics?

Prof. Coen Hemker: Well, that's by the first law of thrombosis and hemostasis. I have called the first law of Thrombosis and Hemostasis as the following:

The more thrombin, the more thrombosis and the less bleeding, and the less thrombin, the less thrombosis and the more bleeding.

Bob Barrett: Professor Coen Hemker is emeritus professor of biochemistry, at the medical facilities of Maastricht, Leiden and Paris and Director of Synapse, a Research and Development Company. He has been our guest in this podcast from *Clinical Chemistry*.

I am Bob Barrett. Thanks for listening!