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PREEMPT'ing Overreliance on Peripheral Blood-Based ColoRectal Cancer Screening

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Guest: Dr. David Wang is a gastrointestinal medical oncologist and translational researcher at the University of Michigan.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett. Colorectal cancer is the second leading cause of cancer death in the United States and 150,000 new cases are diagnosed each year.

Fortunately, effective screening tools can detect disease in the early stages and this early detection has been shown to reduce mortality by 15 to 70% to depending on the method and frequency of testing. However, the percentage of eligible adults who actually undergo screening falls well below the 80% goal set by the American Cancer Society. Reasons for under-screening vary by individual, but generally include opposition to invasive procedures, limited access to medical care, insufficient insurance coverage, or simply a lack of interest.

What if we could change this? What if there were a test that could be performed using a simple blood sample collected as part of a routine doctor's office visit? Would more patients get screened? And if so, what impact would this have on detection and mortality rates?

A perspective article in the March 2026 issue of *Clinical Chemistry* summarizes performance characteristics of several new non-invasive tests and describes their expected impact on the larger landscape of colorectal cancer screening.

Today we're pleased to welcome the article's author. Dr. David Wang is a gastrointestinal medical oncologist and translational researcher at the University of Michigan. He currently leads multi-site interventional trials in esophageal cancer treatment and chemoprevention. So, Dr. Wang, let's start with the basics. What are the currently available screening tests for colorectal cancer?

David Wang: Yeah, there are actually multiple types of colorectal cancer screening tests. I think most people are familiar with stool-based tests, and probably the oldest and most common is what we call fecal occult blood tests, or also known as a guiac test. And this basically uses a biochemical reaction to detect the presence of blood in the stool. The next generation of

that test is called the FIT test, and that stands for fecal immunochemical testing. And that actually looks for, uses an antibody against the heme protein in stool, again, trying to detect blood.

And then there are newer tests such as, probably most commonly known as Cologuard, where it combines detection of blood as well as mutations in certain genes. So those are the three probably most common stool-based tests. The next most common one is actually colonoscopy. I think most people are familiar with that type of test where you have to do a bowel prep a couple days ahead of time and then you get a sedated procedure and then basically visualization of the entire colon using that colonoscopy. The benefit of that is that you can actually remove abnormal lesions. So, it is not only a screening test, but it also is a preventative test.

And a more common test that is done also at the same time is sigmoidoscopy. So that's a flexible sig, allows you to do that in the ambulatory clinic. It doesn't require as much of a prep, but doesn't again visualize the entire colonoscopy. And then what's less common but has come about in the last couple years, are imaging tests such as CT colonography or most people have heard of colon capsule endoscopy.

The availability of those tests vary depending where you are. And the more common ones, such as the stool-based tests, are done more frequently. So those are done annually versus colonoscopy can be done every 10 years in the average risk person.

Bob Barrett: So, doctor, what is the attraction of peripheral blood-based cancer screening tests?

David Wang: That's a great question. We know that cancer screening is effective specifically in colorectal cancer screening. We've actually seen that the evolution of screening, that colon cancer both incidence and mortality has gone down over the last four decades. The national goal of colorectal cancer screening is 80%. Unfortunately, we are way below that. Despite all the different types of tests that I just mentioned, people just don't go and get a colon cancer screening.

Some of the reasons could be because that they are inherently afraid of an invasive procedure. Other times it's really the inconvenience, as I mentioned earlier, that there's this colon or bowel prep that takes several days. You then have to have a sedated procedure, so you have to have someone drive with you to the procedure and it may take you a day or two to recover. That inconvenience factor is huge.

So obviously if you had a peripheral blood test, you can just go in for a regular checkup, get your blood drawn, and there's

really no inconvenience factor there. And most people understand what a blood test is and are willing to undergo it. So, I think the main thing there is that it just increases access and compliance and hopefully would get us closer to that 80% goal rate.

Bob Barrett: What was the PREEMPT CRC trial and what were those main findings?

David Wang: Yeah, so now that we've kind of talked about peripheral blood testing, obviously there are multiple assays on the market and before they can achieve FDA approval, they have to be shown to be effective. So, there is another peripheral blood based colorectal cancer screening test, and that was completed and approved by the FDA about a year ago. But this is a second assay and this assay is manufactured by a company called Freenome. It doesn't have a specific name for an assay yet.

This is looking at what we call methylation of DNA in the blood. The PREEMPT CRC trial was actually a prospective multi-center cross sectional observational study that enrolled patients who were 45 to 85 years of age and who were at what we considered average risk for developing colorectal cancer. They had to be willing to undergo a colonoscopy. So that was the way that the sensitivity and specificity of the tests were going to be determined.

And as I mentioned, they could not be considered high risk. There were a lot of exclusion criteria, including having a first degree relative that had been diagnosed colorectal cancer before the age of 60, at least two first degree relatives who were diagnosed with colorectal cancer at any age, a family history of hereditary gastrointestinal cancer syndrome such as Lynch syndrome or FAP, a personal history of colorectal cancer or colon adenomas, a history of inflammatory bowel disease, the presence of any malignancy within the past five years, and having undergone any other type of screening test in the last several years.

And again, those patients who had met any of those exclusion criteria would have been considered high risk and might have shifted the ability of the test to determine if they had colorectal cancer. So, they basically enrolled over 32,000 patients and these were seen at 201 centers in 49 US states, as well as in the United Arab Emirates. And then what they considered evaluable patients who actually underwent the colonoscopy lowered the number to 27,000. That's still a large cohort of patients. What they found when they went and did the colonoscopy, which was done within 120 days of enrollment. 72 of the patients were found to have colorectal cancer. Over 2,500 of them had what we called advanced precancerous lesions.

Based on the results of the tests, they were able to show a sensitivity of 79% and a specificity of 91%. That actually met what CMS had set as prior criteria. Screening tests from the peripheral blood had to meet at least a sensitivity of 74% and a specificity of greater than 90%. So, in terms of detecting colorectal cancer, that was pretty sensitive and pretty specific.

Bob Barrett: Well finally, Dr. Wang, how would you apply these results?

David Wang: So, the main part about a screening test is obviously to detect cancer, but you also want to be able to detect lesions that are precancerous or ones that are going to lead to cancer, and that is where this trial showed that the assay was not that effective. So, the sensitivity for detecting precancerous lesions was only 12.5%. If you think about it, you'd like to identify a patient who has a lesion that's going to grow and become a cancer and remove it using colonoscopy. That would be preferable than just diagnosing patients with already established cancers, because those patients are already at risk for having micrometastases and have to undergo much more aggressive treatment.

And so I think that's where there has to be some pause about using these tests. I don't think they can replace colonoscopy. However, as we mentioned early in our conversation, the big issue right now is getting to that 80% goal target rate of screening. And if you're using this test as an adjunct to colonoscopy, increasing access to patients who would never undergo colorectal cancer screening, but say, "Okay, I'm willing to go get a peripheral blood draw, and then if I'm found to be at high risk, then would undergo the colonoscopy." I think that's the perfect place where this test fits in right now.

Bob Barrett: That was Dr. David Wang from the University of Michigan in Ann Arbor, Michigan. He wrote a perspective article in the March 2026 issue of *Clinical Chemistry* exploring new tools for colorectal cancer screening. He's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.