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OvaCheck: breakthrough or also ran?

The test for ovarian cancer uses proteomic pattern testing. It looked good in The Lancet two years ago. The results remain unreplicated

BY EMILY ANDREWS

A new type of cancer-detection test seems to be nearing commercial availability in the US and possibly in Canada soon after. It works by a method called proteomic pattern recognition, and is the first of its kind to be close to market.

Called OvaCheck, it's a much-needed test for ovarian cancer. "More than any other kind of cancer, we don't have an early-detection test," says Dr Lisa Dawson, a gynecologic oncologist in St John's, Nfld who is part of the National Ovarian Cancer Association Executive. Most patients are diagnosed with stage III or IV disease, which is often not curable, as opposed to a stage I disease where the survival rates are in excess of 90%.

She explains that the current combined modalities, CA125 (a protein that's elevated in about 80% of women with ovarian cancer but that has a high false-positive rate) and transvaginal ultrasound are still in the large clinical trial phase and have yet to be proven. "So if we're able to identify a screening test which detects ovarian cancer early, it will be very valuable." Still, she's cautious about OvaCheck which she says "has not really been tested sufficiently that I would offer it to my patients."

The method, described in an article in the February 16, 2002 *The Lancet* by Emanuel F Petricoin and colleagues, profiles proteins according to their size and net electrical charge, in a very specialized type of mass spectrometry. A proteomic pattern, the article explains, is the discriminating pattern formed by a small key subset of proteins or peptides buried among the entire repertoire of thousands of proteins represented in the sample spectrum.

A key difference from most other proteomic tests in development is that actual proteins and their functions are not being identified.

Having defined a pattern using blood samples from patients with known ovarian cancer, the researchers tested the ability to recognize cancer in 116 masked samples from women without cancer, with benign disorders and with Stage I-IV ovarian cancer. The analysis correctly classified 63 of 66 (95%) controls as not having cancer and identified all 50 cancer samples (including 18 with Stage I disease). These results represented 100% sensitivity and 95% specificity, they asserted, and a positive predictive value of 94% compared to a positive predicted value of 35% for CA125.

THE DOUBTERS

In subsequent letters to *The Lancet*, researchers took issue with the stated positive predictive value, given that the incidence of ovarian cancer is so low — about 50 per 100,000 post-menopausal women. There are a number of other problems with the research, notes Dr Eleftherios P Diamandis, a clinical biochemist at Mt Sinai Hospital in Toronto, a key one being that attempts to replicate the original results have not been successful.

A report in the February 9, 2004 *The New York Times* cited controversy over the fact that the test is being put on the market through a route that does not require approval by the FDA. In the US, as in Canada, tests done by central laboratories are presently not subject to the same approval process as are tests sold by a central laboratory to other labs as kits. Peter Levine, President, CEO and a co-founder of Correlogic Systems, Inc of Bethsheba, MD — the company that holds the patent on the algorithm used to characterize the pattern — denies accusations of rushing to market prematurely.

"We have not announced the availability of the test," he told *NRM*. "We're still in the validation stage, which is on going." Scale-up, underway for about 14 months so far, is addressing a host of technical and scientific matters, he says.

COMING SOON?

Mr Levine expects research to eventually address issues such as larger patient samples, variations in method of serum collection and handling, discrimination between cancer stages, response to therapeutic interventions and findings in patients with non-ovarian cancer. Results at each stage, he asserts, will be published. Until better test results are available, says Dr Dawson, the most important measure for women worried about ovarian cancer, especially when they have abdominal or bowel symptoms, is to have a pelvic exam. She hasn't yet had patients coming to her requesting OvaCheck, but is sure she will.

Correlogic has licensed the North American rights for OvaCheck to two US-based laboratory services companies, Quest Diagnostics and Laboratory Corporation of America (LabCorp). LabCorp has a presence in two Canadian provinces, Ontario and Alberta, via its subsidiary Dynacare. Pamela Sherry, LabCorp Vice President of Investor Relations, said the company would like to make the test available in Canada after obtaining the necessary approvals.