Emerging Technology List

Breath Test for Detection of Insulin Resistance (Diatest™)

Canadian Coordinating Office for Health Technology Assessment

No. 26 March 2005

Technology: Breath test for the detection of insulin resistance (Diatest™). An earlier CCOHTA publication on the Diatest™ (Emerging Technology List No. 14, April 2002) contains dated information.

Manufacturer: Isodiagnostika Inc. (a division of Isotechnika Inc.), Edmonton AB

Purpose: Diatest™ is a carbon 13 (^{13}C) glucose breath test intended to identify individuals with insulin resistance. Insulin resistance, defined as reduced tissue sensitivity to insulin, causes the body to compensate by producing more insulin.[1] It is found in individuals at risk for developing type 2 diabetes, cardiovascular disease and other disorders. Insulin resistance can be detected many years before the onset of these conditions.[2]

In a recent study, investigators estimated that more than half the US population is overweight or obese and about a half of these individuals have "clinically significant insulin resistance."[3] The Canadian Heart Health Surveys (1986 to 1992) found that 48% of Canadians exceeded a healthy weight standard [defined as a body mass index (BMI) of ≥25].[4]

Current Regulatory Status: Health Canada authorized the licence for Diatest™ in 2001.[5,6] Diatest™ is licensed in Canada for detecting early evidence of insulin resistance and hence the risk for type 2 diabetes (Kathleen Savage, Therapeutic Products Directorate, Health Canada, Ottawa: personal communication, 2004 Oct 19).

Description: Diatest™ is based on the measurement of $^{13}CO_2$ in the breath after a non-radioactive, carbon-13 labelled substrate is orally administered. The person being tested must fast for eight hours before the test. The individual exhales a breath sample into a specimen tube, then swallows a solution that includes carbon-13 labelled glucose. After one and a half hours, a second breath sample is collected in another specimen tube.

The breath samples are analyzed by either mass spectrometry or by infrared spectroscopy. In the first approach, the samples are sent for laboratory analysis that is done with a mass spectrometer. In the second approach, the breath samples are analyzed in the physician's office with a point-of-care infrared analyzer developed by Isodiagnostika (ISOMAX). The ISOMAX infrared analyzer can also be used with other Isodiagnostika breath test kits, which were created for the diagnosis of *Helicobacter pylori* infection, fat malabsorption and lactose intolerance.

Cost: Diatest™ will primarily be available through regional laboratory services, such as Dynacare and MDS. Pricing for the test will be established by these companies. It will likely be similar to the cost of existing ^{13}C urea breath tests used in the diagnosis of *Helicobacter pylori* infection (John Porter, Isodiagnostika, Edmonton: personal communication, 2004 Oct 5). The cost of ^{13}C urea breath tests in Canadian diagnostic laboratories currently range from approximately C$60 to C$80.[7-9] The ISOMAX analyzer for point-of-care testing costs approximately C$20,000 (John Porter: personal communication, 2004 Sep 29).

Evidence:

A small cohort study of 26 adults (10 healthy, non-obese individuals; seven obese individuals; and nine individuals with type 2 diabetes) showed that ^{13}C glucose breath test measurements of insulin sensitivity correlated well with results from hyperinsulinemic euglycemic clamp tests.[10] Investigators found some variability in insulin resistance values and speculated that these may be due to chance or to other factors, such as serum triglycerides, for which they had not accounted. The study results also showed a strong association between body weight or BMI and insulin resistance, though the breath test detected differences in insulin resistance beyond those that could be accounted for solely by body weight. The investigators noted that the performance of the breath test requires further validation under different conditions, such as post-exercise or in patients on medication.

Available Alternative Technologies:

The hyperinsulinemic euglycemic clamp test, also called the insulin clamp test, is the gold standard test for measuring insulin sensitivity. The clamp test involves a complicated and expensive biochemical laboratory procedure and is unsuitable for widespread clinical use. Fasting insulin, glucose and triglycerides blood tests or a combination of tests and risk factors may also be used to determine insulin resistance. The tests and risk factors analysis include the homeostasis model assessment (HOMA) – a mathematical modelling of fasting blood glucose and insulin levels – the calculation of BMI and waist-to-hip ratios, the presence of gestational diabetes or a family history of diabetes.[11]

Breath tests for diabetes and other conditions are being investigated by various companies. For example, Menssana Research is developing a portable analyzer, which captures volatile organic compounds in the breath. Breath samples are analyzed by gas chromatography and mass spectroscopy to detect various markers of oxidative stress, which are associated with different diseases.[12-14] Investigators at Pan Diagnostics in Scotland are also studying breath tests using oxidative stress indicators as markers for various conditions, including diabetes.[15]

Commentary:

Insulin resistance is often discussed as part of a cluster of symptoms related to a "metabolic syndrome" (such as obesity and elevated triglycerides, blood pressure and blood sugar levels) or "prediabetes." Weight loss, dietary changes and lifestyle changes are typically recommended for these conditions. The early detection of insulin resistance may theoretically allow patients to begin preventive interventions intended to delay or avoid the development of diabetes. According to the American Heart Association, "the safest, most effective and preferred way to reduce insulin resistance in overweight and obese people is weight loss and increased physical activity."[16] The actual measurement of insulin resistance in itself is currently used more for research purposes rather than in clinical practice (Dr. Steven Wong, University of British Columbia, Vancouver: personal communication 2004 Nov 15).

Breath tests are non-invasive, easily administered and more acceptable to patients than blood or urine tests. Larger studies are needed to determine whether patients will benefit from the measurement of insulin resistance. Until such information is available, it is difficult to determine the clinical advantage of a test for insulin resistance while other indicators for risk (such as BMI) are available.

Future research may help to identify other roles for this test. The test may have a role in guiding therapy, for example, to determine when to use more expensive drugs (such as thiazolidinediones) in patients for whom initial treatment with less expensive drugs, such as metformin, have failed. It may also be useful in clinical research in identifying a mechanism of poor diabetic control in non-obese patients who may otherwise not be considered insulin resistant (Dr. Steven Wong: personal communication 2004 Nov 15).

References:

1. American College of Endocrinology Task Force on the Insulin Resistance Syndrome. American College of Endocrinology position statement on the insulin resistance syndrome. *Endocr Pract* 2002;9(3):236-9. Available: http://www.aace.com/pub/irscc/IRSGuidelines.pdf (accessed 2004 Oct 6).
2. Rao G. Insulin resistance syndrome. *Am Fam Physician* 2001;63(6):1159-6. Available: http://www.aafp.org/afp/20010315/1159.html (accessed 2004 Oct 6).
3. McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. *Ann Intern Med* 2003;139(10):802-9.
4. Raine KD. *Overweight and obesity in Canada: a population health perspective.* Ottawa: Canada Institute for Health Information; 2004. Available: http://www.cihi.ca (accessed 2004 Oct 21).
5. Edmonton firm unveils diabetes breath test. *Ottawa Bus J* 2001;(June 18). Available: http://www.isotechnika.com/isotechnika_dev/media_details.asp?ID=20 (accessed 2002 Feb 26).
6. *Medical devices active licence listing* [database online]. Rev. Ottawa: Medical Devices Bureau, Therapeutic Products Directorate, Health Canada; 2004 Nov 24. Available: http://www.mdall.ca/.
7. Laboratory medicine. In: *Medical Services Commission payment schedule.* Rev. Victoria: Ministry of Health Services; 2004. Available: http://www.healthservices.gov.bc.ca/msp/infoprac/physbilling/payschedule/31labmed.pdf (accessed 2004 Oct 6).
8. *Urea breath test for helicobacter pylori.* Calgary: Calgary Laboratory Services; 2004. Available: http://www.calgarylabservices.com/LabTests/AlphabeticalListing/U/Urea-Breath-Test-For-Helicobacter-pylori.htm (accessed 2004 Oct 6).
9. Chiba N, Veldhuyzen Van Zanten SJ, Escobedo S, Grace E, Lee J, Sinclair P, et al. Economic evaluation of Helicobacter pylori eradication in the CADET-Hp randomized controlled trial of H. pylori-positive primary care patients with uninvestigated dyspepsia. *Aliment Pharmacol Ther* 2004;19(3):349-58.
10. Lewanczuk RZ, Paty BW, Toth EL. Comparison of the [13C]glucose breath test to the hyperinsulinemic-euglycemic clamp when determining insulin resistance. *Diabetes Care* 2004;27(2):441-7. Available: http://www.isotechnika.com/assets/DiabetesCare_February2004.pdf (accessed 2004 Oct 19).
11. McAuley KA, Williams SM, Mann JI, Walker RJ, Lewis-Barned NJ, Temple LA, et al. Diagnosing insulin resistance in the general population. *Diabetes Care* 2001;24(3):460-4.
12. *About breath tests.* Fort Lee (NJ): Menssana Research, Inc.; 2004. Available: http://www.menssanaresearch.com/btabout.html (accessed 2004 Oct 19).
13. Phillips M, Cataneo RN, Cheema T, Greenberg J. Increased breath biomarkers of oxidative stress in diabetes mellitus. *Clin Chim Acta* 2004;344(1-2):189-94.

14. *Breath tests for diabetes screening* [Health technology forecast]. Plymouth Meeting (PA): ECRI; 2004.

15. *PDL research.* Inverness (UK): Pan Diagnostics Ltd; 2004. Available: http://www.pan-diagnostics.com/breath-analysis-research.html (accessed 2004 Oct 19).

16. *Metabolic syndrome.* Dallas: American Heart Association; 2004. Available: http://www.americanheart.org/presenter.jhtml?identifier=4756 (accessed 2004 Oct 4).

CCOHTA would like to thank Steven Wong, MD, FRCPC, Clinical Instructor, University of British Columbia Postgraduate Medical Education, for his comments on a draft of this summary.

This summary was prepared by Leigh-Ann Topfer; CCOHTA.

This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

These summaries have not been externally peer reviewed.

ISSN 1499-108X (online only)