Metabolic 'breathalyzer' reveals early signs of disease

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The future of disease diagnosis may lie in a "breathalyzer"-like technology currently under development at the University of Wisconsin-Madison.

New research published online in February in the peer-reviewed journal *Metabolism* demonstrates a simple but sensitive method that can distinguish normal and disease-state glucose metabolism by a quick assay of blood or exhaled air.

Many diseases, including diabetes, cancer, and infections, alter the body's metabolism in distinctive ways. The new work shows that these biochemical changes can be detected much sooner than typical symptoms would appear – even within a few hours – offering hope of early disease detection and diagnosis.

"With this methodology, we have advanced methods for tracing metabolic pathways that are perturbed in disease," says senior author Fariba Assadi-Porter, a UW-Madison biochemist and scientist at the Nuclear Magnetic Resonance Facility at Madison. "It's a cheaper, faster, and more sensitive method of diagnosis."

The researchers studied mice with metabolic symptoms similar to those seen in women with polycystic ovary syndrome (PCOS), an endocrine disorder that can cause a wide range of symptoms including infertility, ovarian cysts, and metabolic dysfunction. PCOS affects approximately 1 in 10 women but currently can only be diagnosed after puberty and by exclusion of all other likely diseases – a time-consuming and frustrating process for patients and doctors alike.

"The goal is to find a better way of diagnosing these women early on, before puberty, when the disease can be controlled by medication or exercise and diet, and to prevent these women from getting metabolic syndromes like diabetes, obesity, and associated problems like heart disease," Assadi-Porter says.

The researchers were able to detect distinct metabolic changes in the mice by measuring the isotopic signatures of carbon-containing metabolic byproducts in the blood or breath. They injected glucose containing a single atom of the heavier isotope carbon-13 to trace which metabolic pathways were most active in the sick or healthy mice. Within minutes, they could measure changes in the ratio of carbon-12 to carbon-13 in the carbon dioxide exhaled by the mice, says co-author Warren Porter, a UW-Madison professor of zoology.

One advantage of the approach is that it surveys the workings of the entire body with a single measure. In addition to simplifying diagnosis, it could also provide rapid feedback about the effectiveness of treatments.

"The pattern of these ratios in blood or breath is different for different diseases – for example cancer, diabetes, or obesity – which makes this applicable to a wide range of diseases," explains Assadi-Porter.

The technology relies on the fact that the body uses different sources to produce energy under different conditions. "Your body changes its fuel source. When we're healthy we use the food that we eat," Porter says. "When we get sick, the immune system takes over the body and starts tearing apart proteins to make antibodies and use them as an energy source."

That shift from sugars to proteins engages different biochemical pathways in the body, resulting in distinct changes in the carbon isotopes that show up in exhaled carbon dioxide. If detected quickly, these changes may signal the earliest stages of disease.

The researchers found similar patterns using two independent assays – nuclear magnetic resonance spectroscopy on blood serum and cavity ring-down spectroscopy on exhaled breath. The breath-based method is particularly exciting, they say, because it is non-invasive and even more sensitive than the blood-based assays.

In the mice, the techniques were sensitive enough to detect statistically significant differences between even very small populations of healthy and sick mice.

The current cavity ring-down spectroscopy analysis uses a machine about the size of a shoebox, but the researchers envision a small, hand-held "breathalyzer" that could easily be taken into rural or remote areas. They co-founded a company, Isomark, LLC, to develop the technology and its applications. They hope to explore the underlying biology of disease and better understand whether the distinctive biochemical changes they can observe are causative or side effects.

More information: dx.doi.org/10.1016/j.metabol.2011.12.010

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