



Breathe analysis in disease recognition

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Human breath is a dynamic complex of chemicals in health and disease. Research arena is moving in the direction to identify volatile and non-volatile markers in the exhaled breath to provide clinically useful thought processes. Studies are also inching on the future directions for the prompt point-of-care diagnostic methods of case finding beyond the pulmonary system putting firm footstep in the new millennium. The encouraging results are finding out novel and reliable non-invasive clinical tools to extend the work on in the health and disease, covering the entire gamut of communicable and non-communicable diseases.¹

Globally, in the transitioning of exhaled breath analysis from 'bench side to bed side', the new entrant is relatively poles apart. The mind-set of our fraternity is fixed on the microbiological and serological approaches and has posed as the hindrances for the breathe analysis to contribute in the evidence based medicine. Breathe analysis has traditionally taken two major paths. The original approaches use spectroscopy and other methods to hook and recognize the individual volatile and non-volatile compounds based on broad range of qualitative and quantitative methods. The subsequent researchers are trying to find pattern of changes using the entire mixture of analytes in the exhaled breathe and exhaled breathe condensate without qualitative or quantitative detection of specific compound. These are noninvasive and potentially inexpensive new advances as diagnostic techniques.^{2,3}

Exhaled breathe analysis have inimitable advantages that they can be repeated with time-place and person in contrast to the tests of blood and other body fluid that need to be collected under invasive methods

strictly observing the standard operative procedures observing universal precautions or adherence to time spells as in the collection of urine, stool etc. and, or lack of scope of repetition like imaging techniques or

prohibition of administering several tests in extremes of age groups or in critical care conditions. Further overcoming the portability problem from the fixed to whichever outreach places even in the third world countries, these testing offers real-time point-of-care testing, and it increases the prospective for the upcoming field of activity of 'Family Medicine'.⁴

For the extreme vascularity of the pulmonary system, products of metabolism are abundant in the breathe in varying concentrations. Active pulmonary tuberculosis generates characteristic pattern of volatile breath biomarkers that are sensitive and specific to provide an accurate, rapid, inexpensive and non-invasive diagnostic and prognostic method to distinguish the cases and controls; between those sputum positive or negative for Mycobacteria; also elevated levels in active TB and being reduced with therapy. Up to 130 different biomarkers were consistently detected; the most abundant were naphthalene, 1-methyl-, 3-heptanone, methylcyclododecane, heptane, 2,2,4,6,6-

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pentamethyl-, benzene, 1-methyl-4-(1-methylethyl)-, and cyclohexane. Researchers in different parts of world have been assessing the potential of exhaled nitric oxide from tuberculosis patients with equivocal results.⁵⁻¹¹

Porphyrin and other chemical based colorimetric sensor arrays are being investigated in the world to distinguish between chemically varied compounds based on cross-responsive sensor elements in the prototype of olfactory system of mammals to find biomarkers of cancer and other disease conditions capable of being applied clinically in the near future.^{12, 13}

Indian scientists are working on early diagnosis of pulmonary tuberculosis cases to construct a hand-held, battery-powered sensor with an electric nose technology. For sample collection, patients and healthy subjects are asked to exhale three times—an equivalent of 150 millilitres of breath air—into a specialized air-tight plastic container from where the trapped air is then analyzed; as per their reported information, the sensitivity of their current tool is low and cost-effectiveness not yet determined.^{14, 15} The urease breath test provides the possibility of using exhaled breath samples to diagnose urease-producing microbial species, such as *H. pylori*, TB etc. in human body.¹⁶ Exhaled oxides of nitrogen have long been in use in the management of asthma in diagnosis and monitoring; progress in the detection of lung cancer has been steady.⁴

On the downside, the researchers are facing problems of standardization of tests budding out from a range of variables viz. lifestyle factor variations like diet, addiction, and ambience of infrastructure including sampling methods to resistance from our fraternity oozing from unawareness and sincere approval of novel method of diagnosis and prognosis. Novel tools in sampling, design, standardization, and analytical model in breathe testing have unlimited potential to change the concept of primary level care.⁴

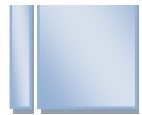
To sum up, recent developments and potential usefulness of exhaled breath analysis by different valid tools and methods need to be internalized with

their progress and success. The breathe tests are basically non-invasive studies and moving in the direction of translating and in search of important new surrogate markers in early bactericidal activity studies of new antibiotics. We have to develop these methods by extensive field studies as they are inexpensive they can take strong roots in the primary care level of the developing world after generating awareness about these non-invasive techniques for diagnosis of different diseases.

The time has come to reconnoitre exhaled breath analysis which is of paramount importance as the successes in non-invasive clinical diagnosis will have a far reaching impact in establishing self-care instruments in futuristic models.

REFERENCE

1. Dweik RA, Amann A. Exhaled breath analysis: the new frontier in medical testing [editorial]. *J Breath Res* 2008; 2(3):1-3.
2. Costa C, Bucca C, Massimiliano B, Solidoro P, Rolla G, Cavallo R. Unsuitability of exhaled breath condensate for the detection of Herpes viruses DNA in the respiratory tract. *J Virol Methods* 2011; 173(2):384-6.
3. Amann A, Corradi M, Mazzone P, Mutti A. Lung cancer biomarkers in exhaled breath. *Expert Rev Mol Diagn* 2011; 11(2):207-17.
4. Mashir A, Paschke K, Laskowski D, Dweik RA. Medical Applications of Exhaled Breath Analysis and Testing. *PCCSU Article* 2011 Electronic nose can sniff tuberculosis. 2012 [online] [cited 2013 April 16] Available from: <http://69.36.35.38/accp/pccsu/medical-applications-exhaled-breath-analysis-and-testing?page=0,3>
5. Bourzac K. New Breath-Based Diagnostic, An MIT Enterprise Technology Review. 2010 Electronic nose can sniff tuberculosis. 2012 [online] [cited 2013 April 16] Available from: <http://www.technologyreview.in/biomedicine/20411/>
6. Marczin N, Kharitonov SA, Yacoub MH, Barnes PJ. Disease markers in exhaled breath. In Part Two: Methodological and Technical aspects; In chapter: Exhaled nitric oxide, carbon monoxide



- and breath condensate. *Lung Biology in Health and Disease*, Volume 170: 290pp.
7. Volatile Markers of Pulmonary Tuberculosis in the Breath. 2011 Electronic nose can sniff tuberculosis. 2012 [online] [cited 2013 January 26] Available from: <http://www.sbir.gov/sbirsearch/detail/229978>
 8. Now There's a Breath Test For Tuberculosis 2010 [online] [cited 2013 March 15] Available from: <http://getbetterhealth.com/now-theres-a-breath-test-for-tuberculosis/2010.03.12>.
 9. Phillips M, Basa-Dalay V, Bothamley G, Cataneo RN, Lam PK, Natividad MP, Schmitt P, Wai J. Breath biomarkers of active pulmonary tuberculosis. *Tuberculosis (Edinb)* 2010; 90(2):145-51.
 10. Van Beek SC, Nhung NV, Sy DN, Sterk PJ, Tiemersma EW, Cobelens FG. Measurement of exhaled nitric oxide as a potential screening tool for pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2011; 15(2):185-92.
 11. Phillips M, Cataneo RN, Condos R, Ring Erickson GA, Greenberg J, La Bombardi V, Munawar MI, Tietje O. Volatile biomarkers of pulmonary tuberculosis in the breath. *Tuberculosis (Edinb)* 2007; 87(1):44-52.
 12. Tuberculosis 2013 [online] [cited 2013 Jan 15] Available from: <http://isensesystems.com/applications/tuberculosis/>
 13. Rakow NA, Suslick KS. A colorimetric sensor array for odour visualization. *Nature* 2000; 406: 710-713.
 14. Handique M. Breath test by Indian scientists promises faster diagnosis of TB. 2013 [online] [cited 2013 Jan 15] Available from: <http://www.livemint.com/Politics/pLEoduzo8fQqMVGWHZAKRO/Breath-test-by-Indian-scientists-promises-faster-diagnosis-o.html>
 15. Electronic nose can sniff tuberculosis. 2012 [online] [cited 2013 April 16] Available from: http://www.thaindian.com/newsportal/sci-tech/electronic-nose-can-sniff-tuberculosis-with-images_100575253.html
 16. Maiga M, Abaza A, Bishai WR. Current tuberculosis diagnostic tools & role of urease breathe test. *Indian J Med Res* 2012; 135(5):731-6.