Conferences

TB diagnostics in India: From importation and imitation to innovation, Bengaluru, 25–26 August 2011

With over 9 million incident cases yearly worldwide and almost 2 million deaths, tuberculosis (TB) continues to be a major public health threat. Progress has been made with the directly observed-treatment, short-course (DOTS) programme, which increased the access to anti-TB therapy. However, in India, despite a large public health effort and 100% DOTS coverage, 2 million cases of active TB disease occur every year. One of the main challenges in controlling the epidemic is the lack of an accurate point-of-care test (POC) for diagnosis. The newly WHO-endorsed test from Cepheid, the Xpert MTB/RIF assay is a big advance, but very expensive. This has stimulated interest in finding more affordable, quicker and simpler TB diagnostic tests.

India has enormous potential in revolutionizing the TB diagnostic landscape along with the other BRICS (Brazil, Russia, India, China, South Africa) countries. The Indian biotechnology sector has developed tremendously over the past decade. However, the obstacles on the road to Indian success in the field of TB diagnostics are manifest as well. One of the main issues, the lack of innovation, was addressed on 25–26 August 2011, at a conference hosted by the St John's Research Institute on 'TB Diagnostics in India: From importation and imitation to innovation'. This conference was aimed at bringing together academia, industry, government, donors and civil society to outgrow the model of 'imitation and importation' and move towards the 'innovation' model (conference website: *http://www.tbevidence.org/rescentre/presentations/bangalore.htm*).

Members of the industry highlighted current barriers to innovation. The most notable barriers were the lack of incentive and capacity to innovate, as well as the need for input from various sectors, notably academia, industry and government. Though the incentive to innovate has increased over the years, the need for competition, encouragement from peers, benefits and rewards remain limited. Technical input, mentorship and guidance are important factors, particularly for companies that are new to the field of TB. Moreover, human resources, funding, infrastructure and knowledge need to be shared between sectors such as academia and government to aid the private sector in investing in innovation.

Representatives of companies expressed concern regarding the true size of the market for TB diagnostics and whether it can cover the financial risk that is necessary to sustain the research and development (R&D) process. A preliminary market analysis was presented by McKinsey, which showed that the market size exceeds US$ 100 million for India alone and could be larger if a new product is launched internationally as well. As the Government of India increases spending on healthcare, more options will also become available for companies wishing to invest in TB diagnostics, such as partnering up with other biotechnology companies, with the government or with academia to enhance their chances of success.

Around half of all funding for R&D in TB diagnostics in past years has been from philanthropic foundations, namely the Bill and Melinda Gates Foundation, while certain individual countries, including India, each contributed only 1% of all TB diagnostics funding. A change in the funding structures is anticipated in the coming years due to the recognition that TB is an important public health problem globally. In India, new funding is expected to be available from the government, national and international philanthropic foundations, international donor agencies, venture capitalists and potential prizes. With the changing landscape of R&D funding for TB diagnostics, larger number of opportunities will be available for companies wishing to invest. When polled, companies expressed that an ideal funding medium would be in the form of a grant, though many were interested in the prospects of competing for an X-prize, when a putative prize for a TB POC test was presented.

Companies expressed the need to have more information on the target product profile that the Revised National Tuberculosis Control Programme (RNTCP) is envisioning for a new diagnostic test. An RNTCP representative described the needs as 'a new POC test that is simple, easy, cheap and capable of being performed with very minimal training'. The RNTCP is also hoping for a cheap, simple, battery-run automated POC molecular test to detect drug resistance, again with minimal training needs. An interesting point was made about providers in the private sector. The RNTCP recognized that they serve at least 50% of the population owing to their convenient geographical location and their ability to offer more personalized and rapid care. Thus, an important need would be to incentivize the private sector to adopt the current and future RNTCP-endorsed diagnostic and treatment course for TB to ensure the efficacy of TB control efforts in India.

An ideal plan to tackle the need for a new POC test would have academia, industry and investors (i.e. venture capitalists, philanthropic foundations, etc.) working together. Academics have the knowledge required to devise a successful POC test, industry has the means to engineer it and investors have the funds. The question is how to make these sectors work together to ensure optimal benefit for all. Though some industry and academia members seem to be getting ready to take on the TB diagnostics challenge, investors are still uncertain that the benefits will be worth the risk. Indeed, the perceived small market size for TB, along with the low margin on sales, the lack of regulations in India as well as potential difficulties in entering a foreign market are all being considered before investments are made in this field.

An important concept discussed was the need to improve the quality standards and enforcement of regulations by putting in place a regulatory system. In India, regulation of diagnostics is weak and several suboptimal TB tests (e.g. serological kits) are on the market. Also, if several TB products were to be developed, it is not clear which agency can do head-to-head validations of these tests. These issues will remain of importance if industry and investors are to provide capital for the development of a new test. It will be important for investors and companies to know the specifications required for a test to be endorsed and adopted by the RNTCP.

The importance of civil society and the media in raising awareness of TB as a major public health threat and the need for a new test were also underscored. Support from civil society campaigns and the media would perhaps be able to mobilize public support and help lobbying to improve R&D for TB diagnostics in India. It could do so by advocating the need for better diagnostics and the use of RNTCP-endorsed tools, as well as by supporting the ongoing research for new technology.

The conference was a first step in bringing together stakeholders in the field of diagnostics research in India. It enabled them to begin a dialogue centred on the problems and solutions needed to work towards an affordable POC for the diagnosis of active TB. One can only hope that the interactions will trigger changes, new ideas and partnerships that enable all those involved to take steps forward in the fight against TB.

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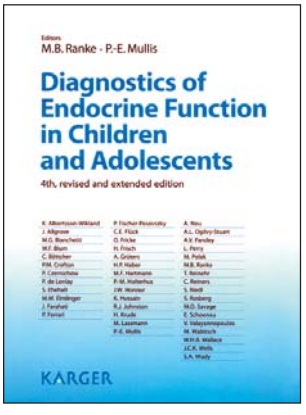
Book Reviews

Diagnostics of Endocrine Function in Children and Adolescents. M. B. Ranke, P. E. Mullis (eds). 4th revised and extended edition. S. Karger, Basel, 2011. *536 pp, US$ 180*. ISBN 978–3–8055–9414–1.



The interpretation of diagnostic endocrine tests is quite complex and needs detailed information both on the subject as well as the procedure. The issue is further complicated in the case of children as changing age, body mass index (BMI) and pubertal status may affect the results of these diagnostic tests. This book is a compilation of the interpretation of these diagnostic tests. This edition has been extensively revised by 43 distinguished European contributors, each recognized as an expert in his or her field. The previous edition was published in 2003; hence, a new edition was very much required to bring the knowledge of paediatric endocrinology up-to-date.

This book presents a range of diagnostic approaches and test procedures used in the evaluation of complex paediatric endocrine disorders. At the same time, the authors have made an attempt to provide normative data on various parameters, especially biochemical, which may help to make the interpretation of results easier. The book has comprehensively reviewed all endocrine diagnostic tests and their interpretation for use in the diagnosis of paediatric endocrine disorders.

The interpretation of diagnostic tests and factors affecting the results of these tests are set out in the text in a nice way, supported by illustrations, graphs and schematic diagrams. However, it would have been better if the cut-off values for the interpretation of these tests had been given in a tabular form or highlighted in a box at the end of the tests to facilitate a quick review. The chapters are organized more or less similarly. All chapters start with an introduction, followed by a brief summary of the disease state and a list of tests to assess endocrine function, with an explanation of the physiological basis. Most of the chapters also include a brief clinical assessment, followed by a detailed endocrine laboratory assessment. Another important feature of the book is that it mentions precautions and correct procedures to collect blood samples for endocrine evaluation—this may be very helpful for practical purposes. Also, it describes the optimum conditions for the storage of blood samples for future evaluation. This will be very useful for people doing research in this area. The authors have also given the normal levels of biochemical parameters according to age, sex and pubertal stage, which is again a very useful inclusion. One of the most difficult and complex issues in paediatric endocrine testing is the use of cut-off values for the interpretation of results. Although it may not be possible for anyone to give clear cut-offs for all the tests, the authors have tried their best to give different cut-offs and have discussed their limitations in view of increasing age. However, at a few places, cut-offs have not been given or discussed, such as in the case of the interpretation of the GnRH stimulation test for the evaluation of the hypothalamic–pituitary–ovarian axis. The reader will thus be forced to search for additional literature on the interpretation of these tests.

In many chapters, the genetic basis of various diseases has been given in a tabular form, which will be of immense help if one wants to do a quick review. The chapter on 'Laboratory measurement of hormones and related biomarkers' is truly exceptional in that it explains all possible details and issues associated with these techniques. It will be very useful in helping the reader to understand the limitations as well as the factors affecting the results of these diagnostic tests. Many chapters from the previous edition have been revised extensively, and newer data have been included. The chapter on insulin resistance will be very useful for researchers as it gives all the practical details of clamp studies. The addition of a new chapter, 'Quantification of densitometric bone parameters and muscle function', is really very valuable as this complex issue is rarely addressed in textbooks. With wider availability of densitometry facilities in India, the interpretation of bone mineral density assessment in children has become important. The format given for the interpretation of the results of densitometry in children is easy to understand; the details of all the terminology used are explained first, and then the interpretation. The relatively recent concept of 'functional muscle-bone unit' is addressed satisfactorily. The details of dysmorphic syndromes associated with endocrine diseases have been compiled