5. Responding to the laboratory bottleneck

The problem

Care of patients with drug-resistant TB starts with a quality assured diagnosis, obtained by growing and identifying *Mycobacterium tuberculosis* from clinical specimens and conducting drug susceptibility testing (DST) of the organism to confirm or exclude resistance. In reality, however, less than 5% of the estimated global burden of MDR-TB cases and an even smaller fraction of XDR-TB cases are being detected, the consequence of critical gaps in laboratory capacity for culture and DST, as outlined in Table 1.

Table 1. Coverage of laboratory services, high-burden countries, 2007

		Population	National reference laboratory (NRL)[a]	Access to diagnostic services						Laboratories included in external quality assurance for sputum smear microscopy	
				Sputum smear		Culture		DST			
		thousands		number of labs	per 100 000 pop	number of labs	per 5 million pop[b]	number of labs	per 10 million pop[b]	number	%
1	*India*	1 169 016	Y	12 184	1.0	11	0.05	11	*0.1*	11 386	93
2	*China*	1 328 630	Y	3 294	0.2	327	*1.2*	187	*1.4*	3 294	100
3	*Indonesia*	231 627	N	4 855	2.1	41	*0.9*	11	0.5	4 855	100
4	*Nigeria*	148 093	Y	794	0.5	2	*0.1*	1	*0.1*	347	44
5	South Africa	48 577	Y	249	0.5	15	1.5	10	2.1	241	97
6	*Bangladesh*	158 665	Y	753	0.5	4	*0.1*	2	*0.1*	753	100
7	Ethiopia	83 099	Y	833	1.0	1	0.1	1	0.1	–	–
8	*Pakistan*	163 902	N	1 131	0.7	3	*0.1*	1	*0.1*	360	32
9	*Philippines*	87 960	Y	2 374	2.7	3	*0.2*	3	*0.3*	2 374	100
10	DR Congo	62 636	Y	1 205	1.9	1	0.1	1	0.2	1 023	85
11	*Russian Federation*	142 499	Y	4 048	2.8	965	*34*	280	*20*	–	–
12	Viet Nam	87 375	Y	737	0.8	17	1.0	2	0.2	–	–
13	Kenya	37 538	Y	930	2.5	5	0.7	1	0.3	37	4.0
14	*Brazil*	191 791	Y	4 044	2.1	193	*5.0*	38	*2.0*	1 819	45
15	UR Tanzania	40 454	Y	717	1.8	3	0.4	1	0.2	–	–
16	Uganda	30 884	Y	716	2.3	3	0.5	2	0.6	716	100
17	Zimbabwe	13 349	Y	180	1.3	1	0.4	1	0.7	0	0
18	Thailand	63 884	Y	1 023	1.6	65	5.1	14	2.2	1 023	100
19	Mozambique	21 397	Y	252	1.2	1	0.2	1	0.5	252	100
20	Myanmar	48 798	Y	324	0.7	2	0.2	1	0.2	54	17
21	Cambodia	14 444	Y	201	1.4	3	1.0	1	0.7	186	93
22	Afghanistan	27 145	Y	500	1.8	1	0.2	–	–	360	72
High-burden countries (22)		**4 201 761**	**20**	**41 344**	**1.0**	**1 667**	**2.0**	**570**	**1.4**	**29 080**	**70**
	AFR	765 283	34	8 547	1.1	110	0.7	45	0.6	4 466	52
	AMR	599 140	29	13 874	2.3	1 487	12	111	1.9	9 040	65
	EMR	555 064	18	4 094	0.7	162	1.5	36	0.6	2 158	53
	EUR	611 415	43	6 744	1.1	2 216	18	762	12	284	4.2
	SEAR	1 745 394	10	20 090	1.2	129	0.4	43	0.2	18 372	91
	WPR	1 648 205	27	7 997	0.5	463	1.4	224	1.4	6 262	78
Global		**5 924 501**	**161**	**61 346**	**1.0**	**4 567**	**3.9**	**1 221**	**2.1**	**40 582**	**66**

– Indicates information not provided; labs, laboratories; pop, population.
a In the lower part of the table the number of countries answering "yes" to this question is shown.
b To provide culture for diagnosis of paediatric, extrapulmonary and ss-/HIV+ TB, as well as DST for re-treatment and failure cases, most countries will need one culture facility per 5 million population and one DST facility per 10 million population.

Arguably the weakest component of health systems, laboratory services have historically been grossly neglected and underfunded. Diagnostic capacity therefore constitutes a major bottleneck for scaling up management and control of MDR-TB and XDR-TB, largely as a result of:

- insufficient and underfunded laboratory strengthening plans;

- inadequate laboratory infrastructure and biosafety;
- vastly inadequate numbers of skilled staff;
- slow diagnostic tool development and technology transfer;
- insufficient and uncoordinated technical assistance.

Estimates based on epidemiological modelling indicate that 60 million culture investigations and five million DST investigations are required annually to meet the diagnostic goals of drug-resistant and HIV-associated TB by 2015, resulting in a current gap of 50 million cultures and 4.5 million DSTs per annum, 85% of these in the high-burden MDR-TB countries. Meeting the estimated global gap will require at least 2,000 new culture and DST laboratories to be established and more than 20,000 new laboratory technicians to be trained and deployed. A systematic approach at country level to planning of laboratory costs is essential, starting with clear policies for screening of patients at risk of MDR-TB and applying appropriate diagnostic algorithms using the different modalities available (solid culture, liquid culture, line probe assays).

Evidence from laboratory assessments shows that the majority of laboratories for culture and DST in resource-limited settings do not meet basic standards for laboratory biosafety or technical proficiency. Standardized operating procedures and quality assurance systems for culture and DST are largely absent or poorly implemented. The high infection risk associated with manipulation of live (and often drug resistant) cultures of *M. tuberculosis* necessitate renovation, construction and maintenance of laboratories according to biosafety level 3 standards, including appropriate laboratory design, negative air flow systems, and validation and maintenance of essential biosafety equipment.

One of the main reasons for the precarious state of laboratory services relates to oversight of and budgets for laboratories often falling outside the jurisdiction of national TB control programmes, thereby aggravating problems relating to laboratory infrastructure, forecasting and planning, and sustainability of technical competency. Human resource development is a particularly pressing problem, with more than 70% of countries reporting critical shortages in skilled laboratory staff. Poor skills distribution, poor compensation, low staff morale and motivation, and lack of career structure being key recurring themes.

Aside from human resources and infrastructure, a major additional impediment to improving and expanding laboratory services is the lack of dedicated, on-site, prolonged, external, experienced technical assistance. The specialized nature of laboratory administration, management and technical procedures dictate the need for specific knowledge and skills, training and mentoring, and ongoing monitoring of performance. Experience shows that training of staff in technical laboratory procedures is relatively easy; however, growing country experience also show that conventional approaches to technical assistance are inadequate, leading to inconsistent technical assistance provided during brief consultant visits, insufficient time devoted to the managerial and administrative components of laboratory strengthening, and poor accountability mechanisms to ensure sustainable quality.

The solution

Research into new TB diagnostic tools has been accelerated over the past few years and the diagnostic pipeline is now rapidly expanding.[1] Commercial liquid culture systems as well as molecular line probe assays for rapid detection of MDR-TB have been recently endorsed by WHO and policy recommendations on their use are available.[2] Technology transfer of these tools has, however, been slow in resource-limited settings as a direct consequence of laboratory services being ill-equipped to absorb these technologies. Robust, point-of-care diagnostic tests for TB are not expected before 2012; therefore, uptake of existing rapid technologies needs to be accelerated and will require adequate, safe laboratory infrastructure and clear policies at country level for their use in MDR-TB screening and diagnostic algorithms.

Adequate laboratory capacity constitutes several essential elements which need to be addressed simultaneously, within comprehensive strategies and national laboratory strengthening plans. Strengthening TB laboratory services may offer one of the best avenues for financing overall laboratory improvement as an essential health systems component. Fundamental to this work is collaboration between TB control programmes and public health laboratory systems at country level, in the areas of:

- Infrastructure, biosafety and utilities
- Human resource development (including training and retention)
- Specimen referral, supply chain management and logistics
- Equipment and maintenance
- Technical procedures (disease-specific)
- Quality assurance
- Data management

Urgent actions needed

- Increased political commitment to strengthening laboratory capacity as an essential health systems component, preferably through a dedicated laboratory directorate or division within the Ministry of Health, with clear management structures, roles and responsibilities;

[1] World Health Organization, Stop TB Partnership Retooling Task Force, Stop TB Partnership New Diagnostics Working Group. *New laboratory diagnostic tools for tuberculosis control*, 2009 (available at www.stoptb.org/retooling).
[2] WHO policy recommendations on the use of liquid culture (2007), second-line drug susceptibility testing (2008) and the use of line probe assays for rapid MDR-TB screening (2008) are available at www.who/tb/dots/laboratory/en.

- National laboratory strategic plans, delineating different levels of laboratory service delivery within tiered laboratory networks and outlining the role of different technologies (including rapid diagnostic tests for drug resistant TB) in screening and diagnostic algorithms;

- National human resource development and training plans, outlining the different expertise required at each level of laboratory services, establishing career paths and appropriate remuneration, and developing strategies for human resource retention;

- Increased and sustained funding from bilateral and multilateral donors to support the essential elements of laboratory strengthening as a cross-cutting health systems component, linked to appropriate monitoring and evaluation mechanisms to avoid duplication and optimize synergies;

- Creation of novel mechanisms for long-term, on-site technical assistance to accelerate the capacity of countries to perform mycobacterial culture, DST and rapid molecular tests within quality assured laboratory systems, tied to a plan for development of sustained local capacity and leadership.

- Increased research on, and funding for, the development and rapid deployment of robust point-of-care diagnostic tests.