APEC CONFERENCE ON PREVENTION, CONTROL AND CARE FOR MDR-TB AND SUPPLY OF 2nd-LINE ANTI-TB DRUG

CHILE

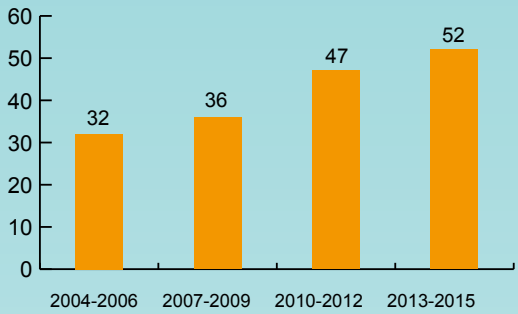
Provided by
Dr. Tania Herrera — Director TB Program, Ministry of Health
Dr. Carlos Pena — TB Program Adviser, Ministry of Health

MDR-TB in Chile

Surveillance MDR-TB

Epidemiological surveillance of MDR-TB is carried out in Chile since the 90s. From 2002 to 2015 they have been 189 cases of MDR-TB, with an average of 13 cases per year, representing less than 1% of total cases of tuberculosis in the country.

MDR-TB cases by triennial. Chile 2004-2015



Primary resistance to anti tuberculosis drugs in Chile

Chile has conducted several initial study of resistance to first line anti tuberculosis drugs as part of the Drug Surveillance Resistance in tuberculosis promoted by the WHO. The last study was carried out in 2011-2012 showing an overall level of TB drug resistance of 8.6% (Table 1) and a prevalence of multidrug resistance of 1.3%.

Since 2014 the monitoring of drug resistance to TB is universally performed to avoid sub - diagnosis and treat each case according to the susceptibility profile.

Table 1: Cumulative prevalence of resistance to first line anti tuberculosis drugs. Chile 2011-2012

Drug	%
Isoniazid	5,1
Rifampin	1,3
Streptomycin	5,9
Ethambutol	0
Pyrazinamide	0,17

A good management of drug sensitive cases is the best prevention of MDR –TB

Strategies to fight against MDR-TB

STRENGHT	AREAS FOR IMPROVEMENT
Universal DST for first- and second-line drugs	Early diagnosis (new diagnostic tools)
Specific treatment for resistance profile	Improve de adherence to sensitive tuberculosis cases
Central committee to decide clinical management	
Centralized drug distribution (not in market)	
Universal cover of DOTS	
Clinical guidelines	

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CHINA

Provided by

Mr. Xiaoqiu Liu Director, the department of policy and program, National Center for Tuberculosis Control and Prevention, China CDC

Mrs. Wei Su Staff, the department of Drug-resistant TB control, National Center for Tuberculosis Control and Prevention, China CDC

Background

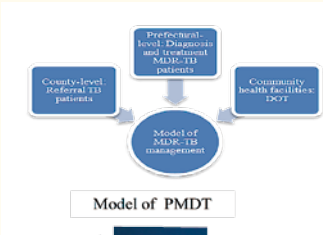
China is estimated to have nearly a quarter of all global MDR-TB patients. We started programmatic management of drug-resistance in 2006, supported by the Global Fund project. Until the end of the Global Fund projects on June 30, 2014, one third of the cities in 30 of the 31 provinces have been covered.

After the end of the Global Fund project, the Chinese government continues to carry out and scale up PMDT with domestic funds.

The mode of PMDT in China is city level responsibility for diagnosis and treatment, county level responsibility for suspected recommendations and community responsibility for the management of patients. The treatment follows the regimen that WHO recommended. The treatment of patients is covered by medical health insurance, the reimbursement ratio is at least 70%. Poor patients will be aided by the Civil Affairs Department.

Accomplishments

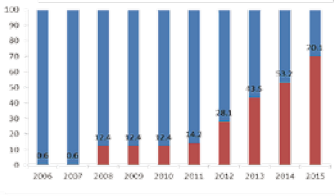
- Issued NTP for the 12th 5-year plan in which the coverage of PMDT at city level reached 50%,the screening rate of MDR-TB high risk groups reached 60%. Actually, we have exceeded the established objectives. Coverage and screening rates were 70% and 74% respectively at the end of 2015.
- Developed some technical documents:
  - Working Guideline for the Programmatic Management of Multi-Drug Resistant Tuberculosis
  - Guideline for MDR-TB Chemotherapy
  - Guideline for Infection Control of Tuberculosis
  - Clinical Pathway of MDR-TB
  - Standardized training series materials for MDR-TB prevention and control (province and prefecture level, county and district level, community and village level)
- Established an internet-based real-time information collection and management system for MDR-TB
- 70% of the cities can carry out the molecular DST with Xpert MTB/RIF and LPAs; nearly a third of the counties can use Xpert MTB/RIF for detection of resistance to rifampicin
- Conducted the National Drug Resistance Surveillance in 2007-2008, the second National Drug Resistance Surveillance is being carried out.



Model of PMDT


TB Management Information System


Technical Documents and Training Materials



The coverage of PMDT in city increased year by year

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INDONESIA

MINISTRY OF HEALTH
REPUBLIC OF INDONESIA

Provided by

Dr. Endang Budi Hastuti
National TB Programme (NTP)

Dr. Endang Lukitosari, MPH
Ministry of Health, Republic of Indonesia

BACKGROUND

Indonesia has implemented Programmatic Management of Drug Resistan TB (PMDT) as the national management system for MDR-TB, stepwisely, started from 2009. The urge to manage MDR-TB can be seen from data of estimated burden TB in Indonesia as shown below:

Table 1 : Estimated Burden of TB in Indonesia 2015
(Global Report, 2015)

Indicator	Level	Total cases of TB per			Rate per 100,000
		Year	Day	Hour	
Prevalence	Global	13,000,000	35,616	1,484	174
	Indonesia	1,600,000	4,384	183	647
Incidence	Global	8,000,000	21,918	913	133
	Indonesia	1,000,000	2,740	114	399
Mortality	Global	1,100,000	3,014	126	16
	Indonesia	100,000	274	11	41
Case Detection Rate, all form					32

Within the data above, particularly estimated burden of MDR-TB and TB-HIV comes out as:

Table 2 : **Estimated Burden of MDR-TB & TB-HIV in Indonesia 2015**
(NTPS 2013 & GTB Report, 2015)

Estimates of DR-TB burden	%	Number
Among new pulmonary TB	1,9 %	5,600
Among relapse pulmonary TB	12 %	1,100
Total		6,700

Estimates of TB-HIV burden	Number	Rate
TB-HIV incidence	63,000	25
TB-HIV mortality	22,000	8,5

CHALLENGES & STRATEGIES

NTP strives to a continued excellence and improvement to overcome the challenges by strengthening the expansion plans strategies as hereby described :

CHALLENGES

1. Slow PMDT expansion and decentralization of services
2. Focus on re-treatment cases, number of testing among new pulmonary TB cases is very low
3. Delays in Xpert expansion, Sputum transport a real bottieneck
4. High loss to follow up (initial LFU and During Treatment LFU)
5. Limited local level support, including socio-economic
6. Surveilance system manual vs eTB manager.

PLANS & STRATEGIES

1. Expansion of PMDT service to district level
2. Building HR capacity in health facilities and in health community to be in line with PMDT expansion Through workshop training cohort review, and clinical and programmatic mentoring
3. Strengthening local capacity in province/district to improve program quality, conducting clinical Supervision in PMDT hospitals and satellites
4. Development and pilot of community-based PMDT care
5. Providing socio-economic support for all MDR-TB patients
6. Improving counselling practice to support PMDT care
7. Regular cohort review in all PMDT sites
8. Building partnership with BPJS to cover MDR-TB treatment cost and side effect management
9. Monitoring the implementation of Bedaquiline and possibility of introducing new drugs and regimen (Delamanid, Shorter Regimen for MDR-TB)
10. Expansion the use of Bedaquiline

Into Indonesia free of tuberculosis, with the spirit of TOSS (Temukan Obati TB Sampai Sembuh-Find, Treat TB until Cured), NTP committed the strategies in accordance with the Global End TB Strategy to reach Zero deaths, disease and suffering due to tuberculosis.

IMPLEMENTATION

TB diagnosis in Indonesia is explained in the algorithm below :

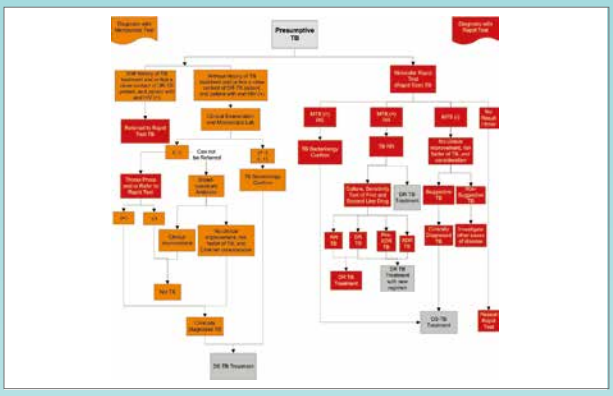
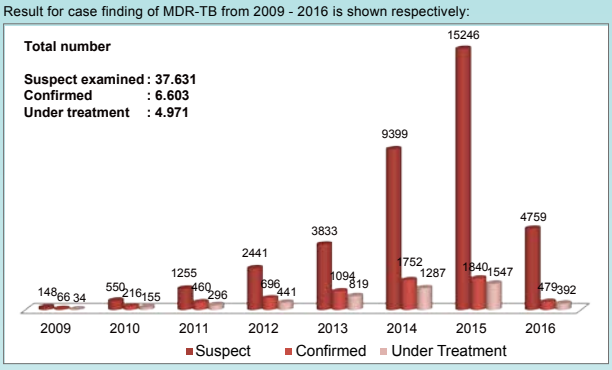


Diagram 1 : Indonesian Algorithm of TB Diagnosis
(NTPS, 2016)

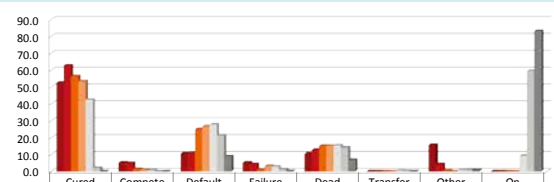
Result for case finding of MDR-TB from 2009 - 2016 is shown respectively:



Graphic 1 : Case Finding of MDR-TB 2009-April 2016
(e-TB Manager Indonesia)

Implementation of PMTD as the management applied for MDR-TB is strengthened with Facilities both diagnostic and treatment & care aspect. Indonesia has 62 Xpert Machines,16Labs for M.TB Culture, 13 Labs certified for 1st line DST, and 5 Labs certified for 2nd Line DST spread over among provinces. Meanwhile support for treatment and care facilities is available as 34 referral hospital for MDR - TB in 31 provinces, 13 sub-referral hospitals, and 1055 satellites facilities that has carried out the services. ±360 units of Xpert Machines are planned to be procured to be allocated in all over the 33 provinces.

Seven years of implementation give raise to the treatment outcome as follows :



	Cured	Compete	Default	Failure	Dead	Transfer	Other	On treatment
2009	52.6	5.3	10.5	5.3	10.5	0	15.8	0
2010	62.9	5.0	10.7	4.3	12.9	0	4.3	0
2011	56.5	1.6	25.1	1.2	15.3	0	0.4	0
2012	53.5	1.2	26.9	3.2	15.3	0	0	0
2013	42.6	0.6	27.8	2.9	15.5	0.4	1	9
2014	2.2	0.0	21.3	1.3	14.1	0.2	1	60
2015	0.0	0.0	9.0	0.2	6.9	0	1	83

Graphic 2 :Treatment Outcome of MDR-TB (%) 2009-2015
(e-TB Manager Indonesia)

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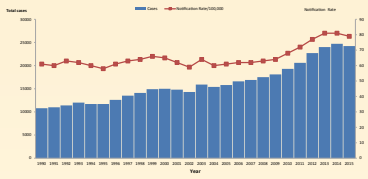
MALAYSIA

Provided by
Dr. Asmah Binti Razali
Public Health Specialist, Division of Diseases Control (TB/ LEPROSY)
Ministry of Health Malaysia

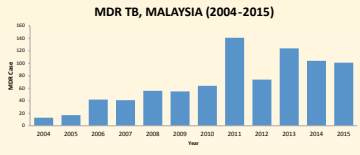
MDR-TB MALAYSIA

TB CASE (ALL FORM) & NOTIFICATION RATE, MALAYSIA (1990- 2015)



	2010	2011	2012	2013	2014	2015
MDRTB Cases	51	141	74	124	104	101
TB Cases	19337	20,666	22,710	23,513	24,079	24,220
(%)	0.3%	0.7%	0.3%	0.5%	0.4%	0.4%

MDR TB, MALAYSIA (2004-2015)



POLICY ON MANAGEMNT OF DR- TB PROGRAMME

- Management of DR-TB is organized around five components like the DOTS strategy, namely:

1. Sustained government commitment
2. Accurate, timely diagnosis through quality assured culture and drug susceptibility testing
3. Appropriate treatment utilizing second-line drugs under strict supervision
4. Uninterrupted supply of quality assured second- line drugs; and
5. Standardized recording and reporting system.

- Prevention is the key to effective control of DR-TB.
  - –MDR-TB arises as a result of improper management of TB patients.
  - –Most cases of XDR-TB arise as a result of poor MDR-TB management.
- To strengthen case holding of patient with TB. DOT supervisors to ensure patient completed TB treatment and cured.
- On-going adherence, counseling and psychosocial support is provided to patients and reinforced throughout treatment.
- Close contacts of patients diagnosed with DR-TB must be screened.
- DR-TB registers should be kept at hospitals and states level (JKN) and updated regularly.

FOCUS AREAS

UP-GRADING LABORATORY FACILITIES

- DR-TB is a laboratory diagnosis and therefore quality-assured laboratory services are importance.
  - – Laboratories doing DST must have internal quality assurance measures in place and participate in external proficiency testing programme.
- Appropriate infection control measures is important to prevent transmission of DR-TB.

TB/HIV COLLABORATIVES ACTIVITY

- All patients with TB and DR-TB will be offered HIV counseling and testing.
- Those who are co-infected should be started on co-trimoxazole and antiretroviral treatment (ART).
- All co-infected MDR /XDR-TB /HIV patients should receive antiretroviral therapy (ART) depending of their CD4 count.

NATIONAL GUIDELINES/ SURVEILANCE DR-TB SYSTEM

- Development of Clinical Practices Guideline for DR-TB in Malaysia; will be national guidance in management of DR-TB.
- Development of DR Tuberculosis Information System; will consist of electronic surveillance for DR-TB cases in Malaysia.

ISSUE & CHALLENGES

- Detection of TB and DR-TB cases in Malaysia
  - –WHO estimated that about 3% of new TB patients in the world would have MDR TB strains.
- Surveillance programme for DR-TB : Programmatic Management of Drug-Resistant Tuberculosis (PMDT) was initiated and will be implemented in the country.
- Nearly 1/3rd (30%) of MDR-TB cases were non Malaysian :Issue with case holding, contact tracing, drug supply and treatment.

- The burden of MDR-TB poses a formidable challenge to the prospect of controlling TB.
- More resources need to be committed in future for TB prevention and control.
- Coverage of DST for TB patients still low and thus a minority of drug-resistant TB patients may not detected and notified.
- Reporting of surveillance and monitoring data DR TB need to improve.
- More budget for research of MDR-TB cases should be allocated.

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MDR-TB AND SUPPLY OF 2nd-LINE ANTI-TB DRUG

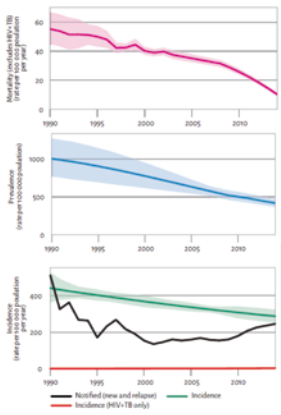
PHILIPPINES

Provided by

Ms. Lucky Cindy Ricafrente — Administrative Officer I, Administrative Service, Department of Health, Philippines

Mr. Jeff Carl Estioco — Senior Health Program Officer, National Capital Regional Office, Philippines

TB Epidemiology



Prevalence Survey, 1983 -2007

Indicator	1983 (1st NTPS)	1997 (2nd NTPS)	2007 (3rd NTPS)
Prevalence of Smear (+)	6.6/1000	3.1/1000	2.0/1000
Prevalence of Culture (+)	8.6/1000	8.1/1000	4.7/1000

Drug Resistance Survey

Indicator	2003	2012
MDR TB among new	4%	2%
MDR TB among re-treatment	21%	21%

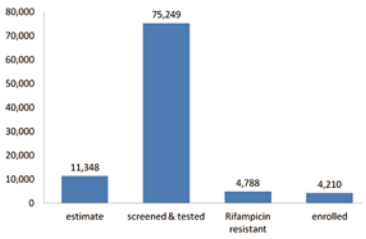
National TB programme

8 Strategies of PhilPACT

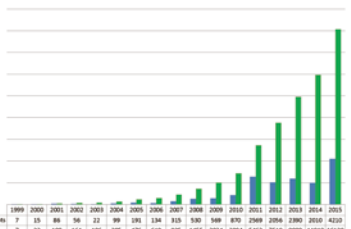
1. Localize TB control program implementation
2. Monitor health system performance
3. Engage both public and private TB care providers to adopt DOTS
4. Promote and strengthen positive TB behavior of communities
5. Address MDR-TB, HIV-TB co-infection and needs of vulnerable populations
6. Regulate and make available quality TB diagnostic tests and anti-TB drugs
7. Certify and accredit TB care providers
8. Secure adequate funding and improve efficiency of fund utilization

- Updated National Strategic Plan (2010-2016 Philippine Plan of Action to Control Tuberculosis)
- Total needed budget for 6 years is Php 29 B (U$ 620 M) with a gap of Php 8 B (U$ 169 M)
- With 8 strategies adopted from the global and regional strategies
- With existing GF grant (2014-2016); with approved 1 year extension (2017)
- In the process of formulating the 2017-2022 National Strategic Plan (NSP)
  - Joint Program Review (March 2016)
  - Drafting of NSP (Q3, 2016)

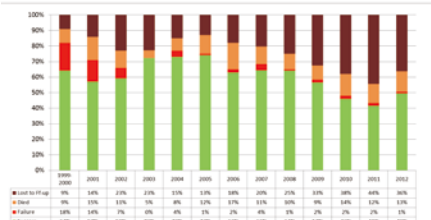
Cascade for PMDT Care



Enrolled Drug Resistant TB Cases, Philippines, 1999-2015



Treatment Outcome of MDR-TB Cases, Philippines, 1999-2012



Strategies for PMDT

- Establishment of PMDT diagnostic facilities: culture centers (24), DST centers (5), and Xpert sites (159); microscopy centers (2,565)
- Scale-up of PMDT treatment facilities: Treatment Centers (20), Satellite TCs (108)
- Integration of PMDT policies and procedures with the basic DOTS at local public health facilities (iDOTS- 284)
- Public-Private Partnership
- Provision of enablers to MDR-TB patients
- Active casefinding among high risk and vulnerable groups

PMDT Expansion

Year	Regional Expansion (17 Regions)	New Tx Facility (TC/STC)	New Xpert Site
2003-2007	NCR	5	
2008	Region 7	1	
2009	Regions 1, 4A, 5, 10, 11	5	
2011	CAR, 6, 9, 12, CARAGA	15	16
2012	Region 4B	12	17
2013	Regions 2, 3, 8	6	24
2014	ARMM	10	10
2015	All regions with access to PMDT services	66	53

Ongoing Researches

9-Month Treatment Regimen

(4HZEKmMfxPtoCfz / 5ZEMfxCfz)

- Piloted in 10 PMDT treatment facilities in July 2015
- As of June 2016: 154 MDR-TB patients enrolled
- Implementation review will be done in August 2016

Bedaquiline Operational Research

- Started May 2016
- Implemented in the 9-MTR study sites also

Challenges and Lessons Learned on MDR-TB Implementation

Challenges

- **Low TSR due to high lost to follow-up and deaths**
- **Sustainability since fully funded by GF**
- **Gap in detection and treatment of cases**

Lessons learned

- **Services should be closer to the patients**
- **Advocacy is important to expand PMDT services down to the communities**
- **Diagnostic and treatment services should be harmonized**
- **All levels of health care should be involved**

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SINGAPORE

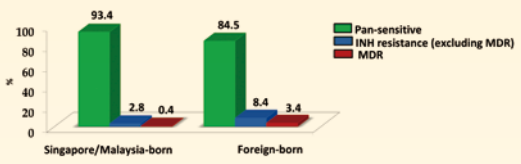
Provided by
S H Gan[1], K M Kyi Win[1], C B E Chee[1], J Cutter[2], Y T Wang[1]
[1]TB Control Unit, Tan TockSeng Hospital, Singapore;[2]Ministry of Health, Singapore

Multi-drug Resistant Pulmonary Tuberculosis in Singapore, 2002-2015

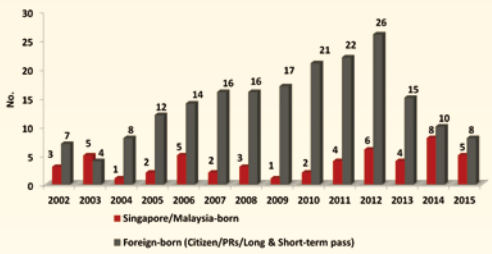
Introduction

The Singapore Tuberculosis Elimination Programme(STEP) was launched in 1997.
The main aim of STEP is to eliminate TB in Singapore by
1)detecting, diagnosing and treating all infectious TB cases
2)identifying and treating infected tuberculosis contacts
3)preventing the emergence of multi-drug resistant tuberculosis.

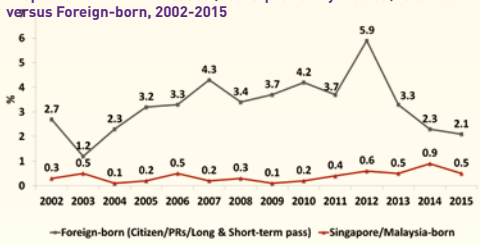
Proportion of Pulmonary TB (PTB) cases with drug-resistance, Local-born (Singapore/Malaysia) versus Foreign-born, 2002-2015



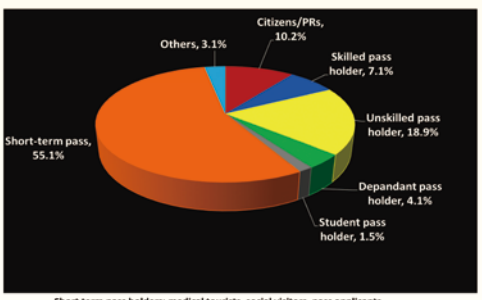
Number of MDR-PTB cases (new & previously treated)Local-born (Singapore/Malaysia) versusForeign-born, 2002-2015



Proportion of MDR-PTB cases (new & previously treated)Local-born versus Foreign-born, 2002-2015

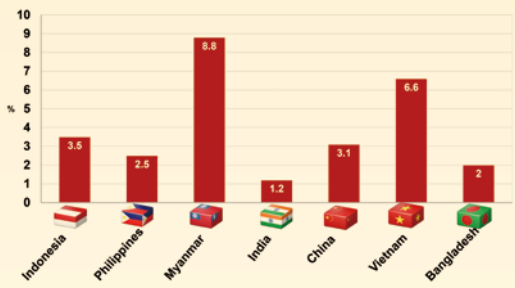


Distribution of MDR-PTB in foreign-born by visa pass status, 2002-2015

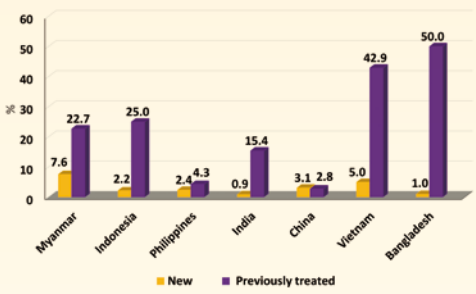


Short term pass holders: medical tourists, social visitors, pass applicants

Proportion of MDR-PTB among foreign-born culture positive PTB cases (new & previously treated) by country of birth, 2002-2015



Proportion of MDR-PTB among foreign-born culture positive PTB cases by country of birth and case category, 2002-2015



XDR-PTB by country of birth, 2002-2015

To date, there has been 9 XDR-PTB cases diagnosed among foreign-born, but not yet to be reported in local population

Drug susceptibility results of MDR-PTB by country of birth2002-2015

Drug Resistance	Myanmar N=48	Indonesia N=73	Philippines N=18	India N=7	China N=33	Vietnam N=11	Bangladesh N=8	Saudi Arabia & Tonga N=2	Singapore/Malaysia N=51
HR only	6.3 (n=3)	17.8 (n=13)	33.3 (n=6)	14.3 (n=1)	9.1 (n=3)	0	0	50.0 (n=1)	29.4 (n=15)
HRS/HRE/HRZ/HRSZ/HRSE/HRSEZ/ >HR with Ethio/PAS/Clofazamine	81.3 (n=39)	57.5 (n=42)	66.7 (n=12)	85.7 (n=6)	81.8 (n=27)	72.7 (n=8)	75.0 (n=3)	0	68.6 (n=35)
Pre-XDR (Fluroquinolone or Injectable)	12.5 (n=6)	16.4 (n=12)	0	0	6.1 (n=2)	9.1 (n=1)	25.0 (n=1)	50.0 (n=1)	2.0 (n=1)
XDR (Fluroquinolone & Injectable)	0	8.2 (n=6)	0	0	3.0 (n=1)	18.2 (n=2)	0	0	0
At least 4 first-line drugs	66.7 (n=32)	37.0 (n=27)	11.1 (n=2)	42.9 (n=3)	51.5 (n=17)	81.8 (n=9)	75.0 (n=3)	50.0 (n=1)	23.5 (n=12)

Strategies

Early detection of drug resistant TB and treatment with appropriate regimen is important in reducing transmission in the community.

Use of GeneXpert test in patients with high risk of drug resistance aids in early detection of MDR-TB.

THAILAND

Provided by
Ms. Saijai Smithtikarn
Chief of NTRL, Bureau of Tuberculosis, Department of Disease Control, Ministry of Public Health

MDR-TB Management in Thailand

Background

Of all new global TB cases, 58% occurred in South-East Asia and Western Pacific Regions. Thailand as a country in South-east Asia has a very long history of TB problem. In 2014, Thailand was estimated to have TB prevalence at about 236/100,000 populations. Approximated number of new cases were at about 120,000 cases (171/100,000 populations). For several years, Thailand has been classified as a country in the list of countries having high burden of TB cases. In 2015, Thailand was also classified to be country that has high burden of MDR-TB and TB- HIV co-infection. Therefore, Thailand has been a country in a list of 14th high burden country-lists in TB. The drug-resistance surveillance (DRS) is a crucial source of information monitored the trend of the situation. Latest round of surveillance in 2012 revealed that MDR-TB were 2.03% in new TB cases. This figure increased from 0.93 % and 1.65 % observed in the year 2001 and 2006, respectively.

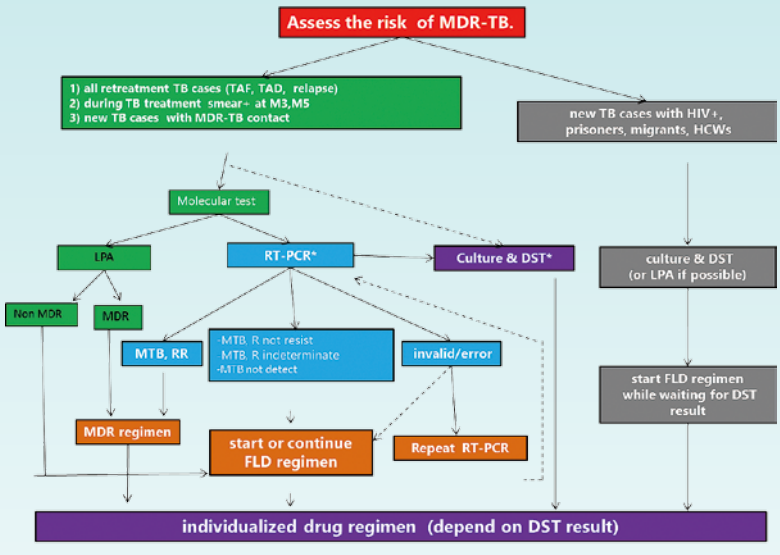
One of challenges in MDR-TB management was low coverage of case finding. The clear algorithm of diagnosis and treatment was in need. The Thailand NTP started working with experts from various universities to develop the guideline and supported the programmatic management.

Accomplishment

Thailand has had a National committee of DR-TB specialists who developed the national MDR-TB guidelines and has been responsible for approval on drug regimen to treat XDR-, pre-XDR-, and difficult-to-treat MDR-TB patients.

The DR-TB guidelines provide the clear algorithm (shown in the figure) that is successfully implemented. This resulted in early diagnosis and the coverage of MDR-TB diagnosis gradually increases. Previously the National Health Security Office found approximately 400 MDR-TB cases on treatment each year, then in 2015 the number of cases increasing to 700 cases.

The DR-TB expert committee has another task on analyzing the history of patients and proactively searching for the appropriate drugs before the treatment start. Adherence to the treatment is continuously monitored.



Algorithm of MDR-TB diagnosis and treatment, Thailand