Case-based Discussion
Multidrug-Resistant Tuberculosis (MDR-TB)

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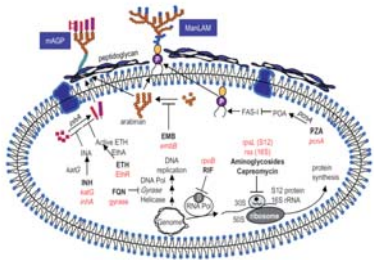
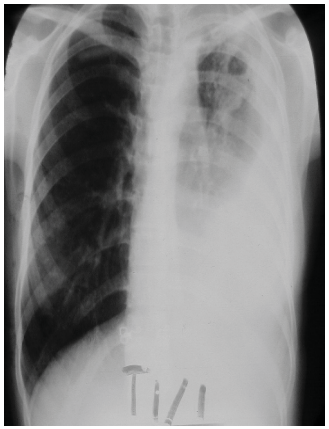


Infectious Disease Association of Thailand Meeting
October 24th, 8.00-8.50 AM

Case Presentation 1

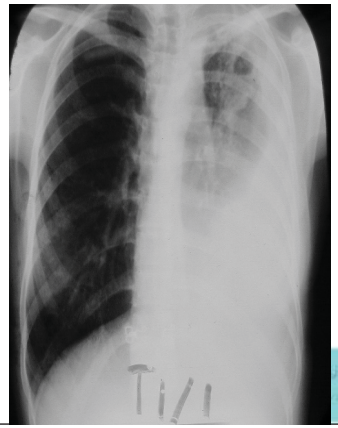
- **A 30-year-old woman, T1DM for 15 years**
- **She developed smear-positive pulmonary TB (PTB)**
- **After treatment with 2 HRZE, her symptoms were improved but sputum smears is 1+ (formerly 3+)**



What will you do next?

Case Presentation 1

- **She received anti-TB under DOT at health-center with good compliance**
- **Her DM control was well, FPG 120-150 mg/dL and HbA1C 6.5-7.0%**
- **Initial sputum culture with drug susceptibility testing (DST) was not performed due to being new case without MDR-TB risks**
- **Follow-up CXR was slightly improved**



Can Serial Qualitative PCR Monitoring Predict Outcome of PTB Treatment?

Chierakul N, et al. Respirology 2001; 6:305-9.

53 patients with PTB, non-HIV, drug-sensitive,
23 female , 4 DM, 31 had cavity, 14 had extensive disease

	8 weeks	16 weeks	24 weeks
Culture +	15	-	-
Smear +	41	11	-
PCR +	53	21	7

- **4 PCR persisters after complete treatment, 1 had slow smear and culture conversion and do relapse 6 months later**
- **Presence of cavity and extensive disease can determine smear persisters at 8 weeks (RR 3.23 and 2.11, p 0.04 and 0.03) but not for culture conversion**

Sputum Monitoring for Predicting TB Outcome

- Systematic review and meta-analysis found low sensitivity and moderate specificity for prediction of relapse or failure
- Poor PPVs, positive sputum result during treatment does not imply that an individual will experience a poor outcome
- Good NPVs indicate that a negative smear or culture examination during treatment implies that an individual will be unlikely to experience treatment failure or relapse

Lancet Infect Dis 2010; 10: 387-394

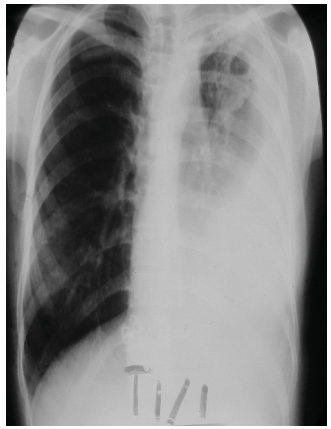
Extension of the Intensive Phase

- 16,708 PTB patients from India, 12,967 were converted at 2 months (2M−)
- 1,871 and 1,870 2M+ were randomised extension or not
- Extension significantly reversed the RR of relapse from 2.2 (95%CI 1.6–3.0) to 0.7 (95%CI 0.4–1.2)
- RR for failure remained 7.3 (95%CI 4.7–11.5) with and 4.2 (95%CI 2.5–7.2) without extension
- More MDR-TB was found after extension, but acquired RMP resistance was similar in all arms
- Sensitivity of the 2-month smear for failure prediction or relapse is 40%, with positive predictive value of 3%

Int J Tuberc Lung Dis 2012; 16:455-461

Case Presentation 1

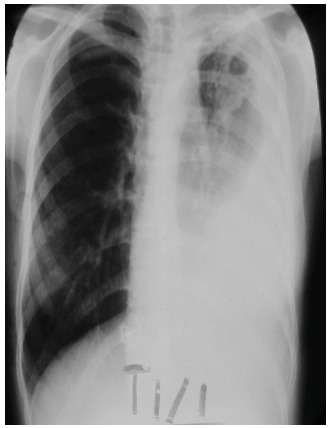
- After 2 HRZE / 1 HR, she remained well, but the follow-up sputum smears revealed few AFB



What will you do next?

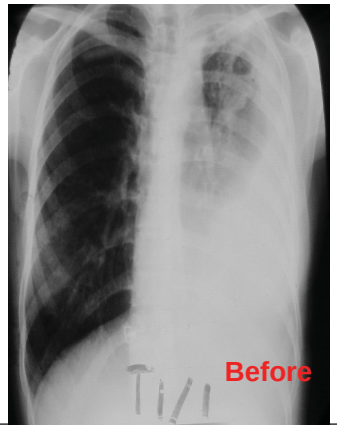
Case Presentation 1

- After 2 HRZE / 1 HR, she remained well, but the follow-up sputum smears revealed few AFB
- Culture and DST was performed, current regimen was continued
- Rapid molecular-based method was not performed due to scant AFB and low clinical suspicious for MDR-TB

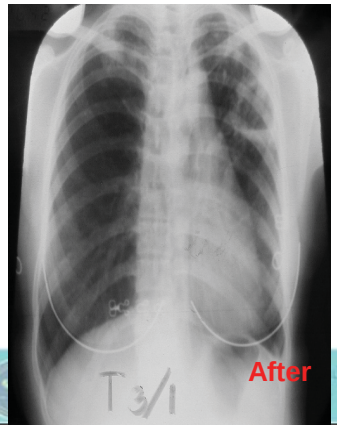


Case Presentation 1

- After 2HRZE / 2HR and good glycemic control, sputum was converted, sputum cultures at 3 months were negative
- After complete 6-month regimen, her post-treatment CXR showed significant residual lesions, the treatment was stop



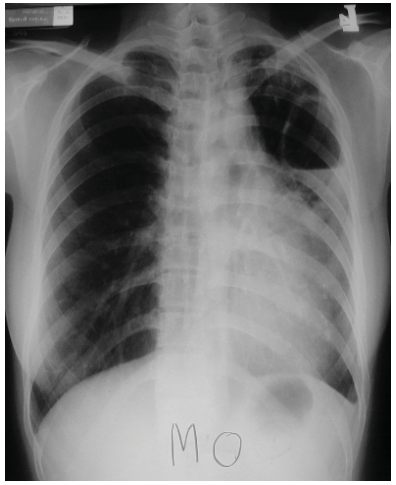
Before



After

Case Presentation 1

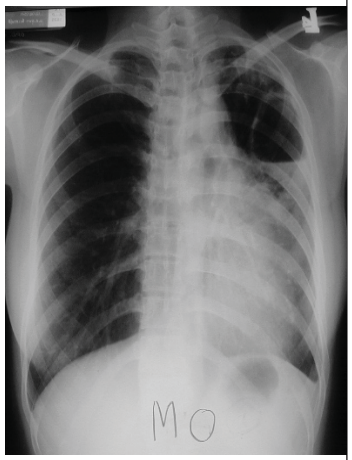
- Her compliance for DM treatment was poor during this year
- 3 months ago, she developed relapse PTB (AFB 3+)



What will you do next?

Case Presentation 1

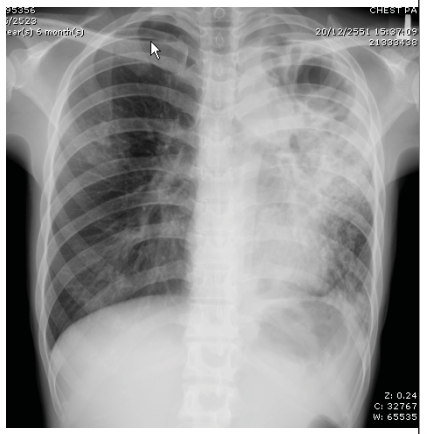
- Her compliance for DM treatment was poor during this year
- 3 months ago, she developed relapse PTB (AFB 3+)
- Culture with DST was sent, rapid molecular-based method was not performed due to low possibility for MDR-TB
- Retreatment regimen (2 SHRZE / 1 HRZE/ 5 HRE) was planned
- After 3 months of treatment, she was slightly better, but the follow-up sputum smear was 2+



What will you do next?

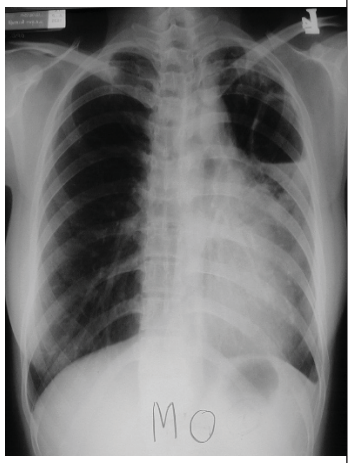
Consideration Before Announcing DR-TB

- Delayed bacilli clearance
- NTM infection or colonization after treatment
- Radiographic prejudice
- Paradoxical response or IRIS
- Laboratory errors



Case Presentation 1

- 3 months ago, she developed relapse PTB (AFB 3+)
- After 2 SHRZE / 1 HRZE, she was slightly better, but the follow-up sputum smear was 2+
- CXR was not improved, initial cultures were contaminated
- Xpert MTB-RIF was equivocal



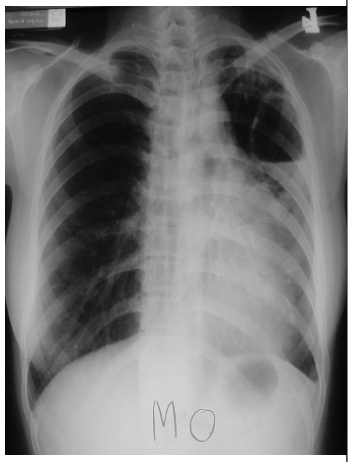
What will you do next?

Standard Regimens for Retreatment Cases

Test	Likelihood of MDR	
DST for all previously treated patients	High (failure)	Medium or low (relapse, default)
Rapid molecular methods	Available in 1-2 days to confirm or exclude MDR	
	Empiric for MDR 6KmLfxEtoCs(±PAS)/≥14LfxEtoCs(±PAS) (9SLfxEtoCsZ/9LfxEtoCs) Modified once DST results are available	2HRZES/1HRZE /5HRE

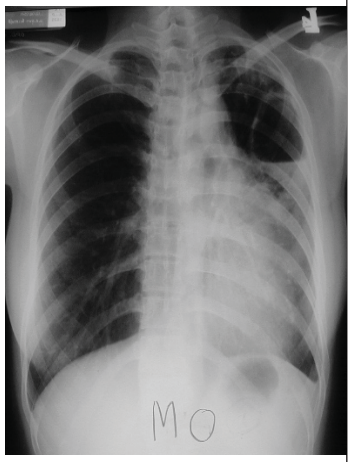
Case Presentation 1

- 3 months ago, she developed relapse PTB (AFB 3+)
- After 2 SHRZE / 1 HRZE 3, she was slightly better, but the follow-up sputum smear was 2+
- CXR was not improved, initial cultures were contaminated
- Xpert MTB-RIF was equivocal
- Repeat Xpert MTB-RIF was positive for *rpoB* gene mutation
- Treatment failure regimen was planned [6 KmLfxEtoCsZ/14 LfxEtoCs(Z)]



Case Presentation 1

- Repeat Xpert MTB-RIF was positive for *rpoB* gene mutation
- Treatment failure regimen was planned [6 KmLfxEtoCsZ/14 LfxEtoCs(Z)]
- After 2 months of treatment, smear-conversion was achieved, DST revealed MTB isolates with H, R, and Z resistance, but E, Km, Lfx, Eto, and Cs sensitivity



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- Regimen was adjusted to Km,Lfx,Eto,Cs,PAS
- After 3 months, cultures at 2 months was positive

What will you do next?

Case Presentation 1

- Repeat Xpert MTB-RIF was positive for *rpoB* gene mutation
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- After 2 months of treatment, smear conversion was achieved, DST revealed MTB isolates with H, R, and Z resistance, but E, Km, Lfx, Eto, and Cs sensitivity
- Regimen was adjusted to Km,Lfx,Eto,Cs,PAS
- After 3 months sputum smears were negative but cultures at 2 months were positive
- Adherence to TB and DM therapy was good, her symptoms became less with 5-kg weight gain

What will you do next?

Case Presentation 1

- Regimen was adjusted to Km,Lfx,Eto,Cs,PAS
- After 4 months, cultures at 3 months were negative
- After complete initial intensive phase for 6 months, monthly sputum cultures were still negative, regimen was tailored to Lfx,Eto,Cs,PAS
- At 9 months, she was still in good health, but the follow-up sputum smears were 1+

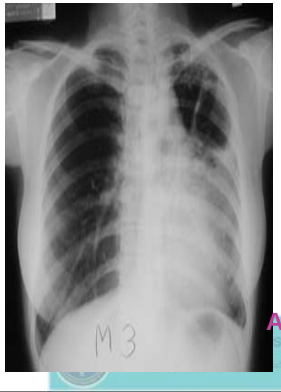
What will you do next?

Case Presentation 1

- After complete initial intensive phase for 6 months, monthly sputum cultures were still negative, regimen was tailored to Lfx,Eto,Cs,PAS
- At 9 months, she was still in good health, but the follow-up sputum smears were 1+
- Line-probe assay was negative for aminoglycoside and quinolone resistance

What will you do next?

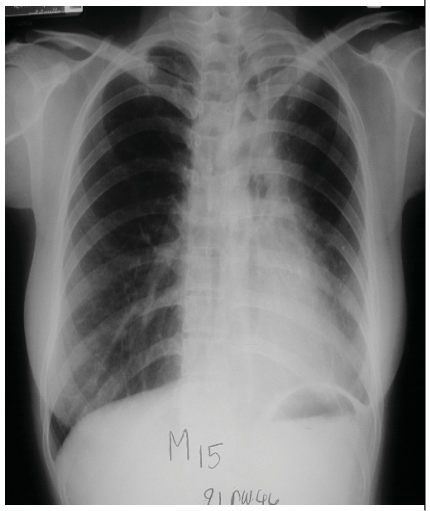
Before



After

Case Presentation 1

- After complete initial intensive phase for 6 months, monthly sputum cultures were still negative, regimen was tailored to Lfx,Eto,Cs,PAS
- At 9 months, she was still in good health, but the follow-up sputum smears were 1+, line-probe assay was negative for aminoglycoside and quinolone resistance
- Chest CT-scan revealed huge cavity nearly occupied the whole left upper lobe, the rest of lung parenchyma was unremarkable, virtual reconstruction demonstrated no significant bronchostenosis
- DST showed non-XDR isolates
- Left upper lobectomy was performed with uneventful clinical course, the regimen is continued until 12 months after surgery with persistent negative cultures



เชี่ยวชาญศาสตร์สรรพ์ ยึดมั่นคุณธรรม ชี้นำสังคม

Consideration for MDR-TB Care

- ART should be co-administered as early as possible, even if IRIS develop
- Hospital-based or community-based site of care is depend on bed availability and patient or care-giver preference
- Adjunctive lung resection in those
  - High probability of failure or relapse
  - Localized disease and acceptable reserved
  - Sufficient drug activity for complete sterilizing during postoperative period

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