Early treatment of MAC lung disease

단국대학교 박재석

Compared to pul. TB

MAC lung ds.

- Present in environment
- Less severe clinical course
- More difficult to tx.
- Poor response to tx.

An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases

Am J Respir Crit Care Med 2007;175:367-416

- Making the diagnosis of NTM lung ds does not mean the initiation of therapy

- Decision of therapy based on potential risk and benefit of therapy for individual patients

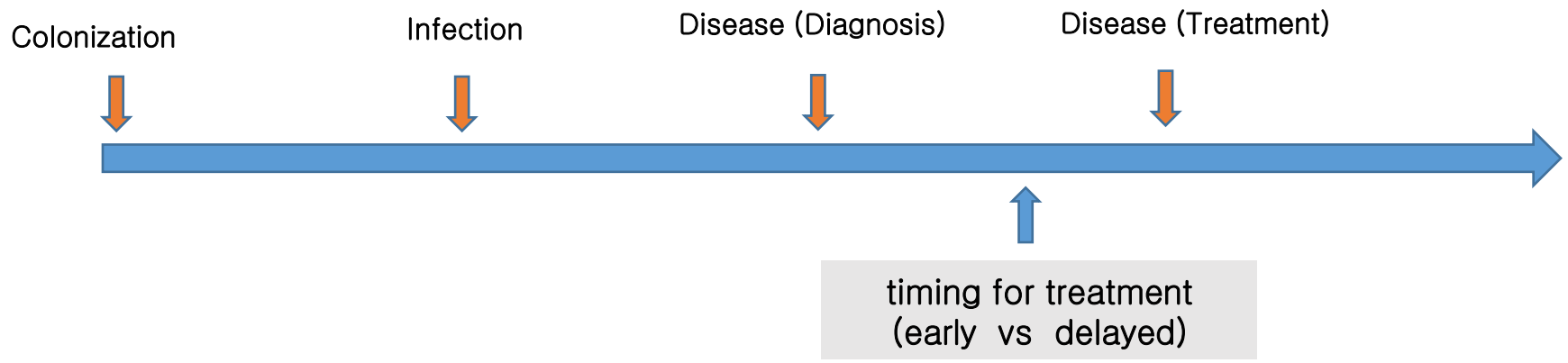
Natural course of MAC lung disease

- Japan, 1999-2005, 117 MAC lung ds.(2007 ATS criteria)
- 5 yr follow up, from the time of diagnosis
  - 54(46%) treated
  - 63(54%) not treated
    - 24 did not experience sputum culture conversion (chronic infection)
    - 39 sputum culture conversion (colonization)

INT J TUBERC LUNG DIS 16(3):408–414, 2012 The Union

Decision of timing for treatment of MAC lung Disease

(Cost-benefit assessment)



- Cost
  - Difficult to tx
    - Long duration of treatment
    - Adverse drug reaction
    - High cost
  - Development of drug resistance

- Benefit
  - Improve clinical symptoms and signs
  - Preserve lung function
  - Bacteriologic Response to tx (bacterial conversion, reinfection..)

Natural course of MAC lung disease if untreated

- Fibrocavitary form
  - generally progressive, and if left untreated can lead to extensive lung destruction and death.
  - Immediate treatment ?
- Nodular bronchiectatic form
  - tends to have a much slower progression than fibrocavitary disease.
  - Even with this more indolent form of disease, progression can occur.

Am J Respir Crit Care Med 2007;175(4):367–416

MAC lung disease

- Japan, 1999-2005, 117 MAC lung ds.(2007 ATS criteria)
- 5 yr follow up, from the time of diagnosis
  - 54(46%) treated
  - 63(54%) not treated
    - 24 did not experience sputum culture conversion (chronic infection)
    - 39 sputum culture conversion (colonization)

INT J TUBERC LUNG DIS 16(3):408–414, 2012 The Union

Table 1 Characteristics and outcomes of patients with pulmonary MAC disease

Radiologic findings	Treated	Chronic infection	Colonization
Cavitary lesion (23)	15 (65%)	5 (22%)	3 (13%)
Bronchiectatic lesion (62)	35 (56%)	11 (18%)	16 (26%)

MAC lung disease(Response to treatment)

- Korea, 2003-2006, 96 MAC lung ds.
- Macrolide based standardized combination tx (>12mo after conversion),
- f/u after completion of therapy : median 6.5 mo

Treatment responses	No. (%) of patients
Symptomatic responses (n = 95)*	
Improved	77 (81)
Unchanged	8 (8)
Worsened	10 (11)
Radiographic responses on HRCT (n = 87)†	
Improved	68 (78)
Unchanged	10 (12)
Worsened	9 (10)

Yonsei Med J. 2010 Nov 1; 51(6): 888-894

MAC lung disease(Response to treatment)

- Korea, 2003-2006, 96 MAC lung ds.
- Macrolide based standardized combination tx (>12mo after conversion),
- f/u after completion of therapy : median 6.5 mo

Microbiologic response

- Favorable microbiologic response : 72(79%)
  - Sputum conversion and maintain > 12 mo
- Unfavorable microbiologic response : 20(21%)
  - Failure to sputum conversion 13
  - Relapse 3
  - MAC related death 4

Yonsei Med J. 2010 Nov 1; 51(6): 888–894

Predictors of favorable microbiologic response

Patient characteristic	Favorable response (n = 76)	Unfavorable response (n = 20)	Univariate analysis	Multivariate logistic regression	
			p value	*p* value	OR (95% CI)
Age > 50 yrs	59 (78%)	17 (85%)	0.470	0.662	1.43 (0.29 - 7.07)
Gender, female	50 (66%)	6 (30%)	0.004	0.065	0.24 (0.06 - 1.16)
Body mass index < 18.5 kg/m²	19 (25%)	8 (40%)	0.184	0.253	2.09 (0.59 - 7.37)
Comorbidity	17 (22%)	7 (35%)	0.246	-	-
Current or former smoker	15 (20%)	9 (45%)	0.020	0.426	1.92 (0.38 - 9.65)
Mycobacterium intracellulare	41 (54%)	15 (75%)	0.089	0.113	2.76 (0.79 - 9.66)
Upper lobe cavitary form	18 (24%)	8 (40%)	0.144	0.410	1.80 (0.45 - 7.23)
Nodular bronchiectatic form	51 (84%)	10 (17%)	0.157	-	-
No. of involved lobes o- HRCT > 5*	24 (32%)	5 (25%)	0.569		
Positive sputum AFB s					
Combined use of strept					
Stopped use of ethambu					
Dose reduction of clarit					

Radiologic findings	Favorable	Unfavorable
Upper lobe Cavitary (26)	18 (69%)	8 (31%)
Nodular Bronchiectatic (61)	51 (84%)	11 (18%)

Yonsei Med J. 2010 Nov 1; 51(6): 888–894

Microbiologic response

- Favorable microbiologic response : 76
  - Sputum conversion and maintain > 12 mo
- Unfavorable microbiologic response : 20
  - Failure to sputum conversion (13), Relapse (3), MAC related death (4)

MAC lung disease (Response to treatment)

- USA, 180 nodular-bronchiectatic MAC lung ds.
- Treated > 12 mo. Mean f/u off therapy : 42mo
- Genotyping prior and during tx.

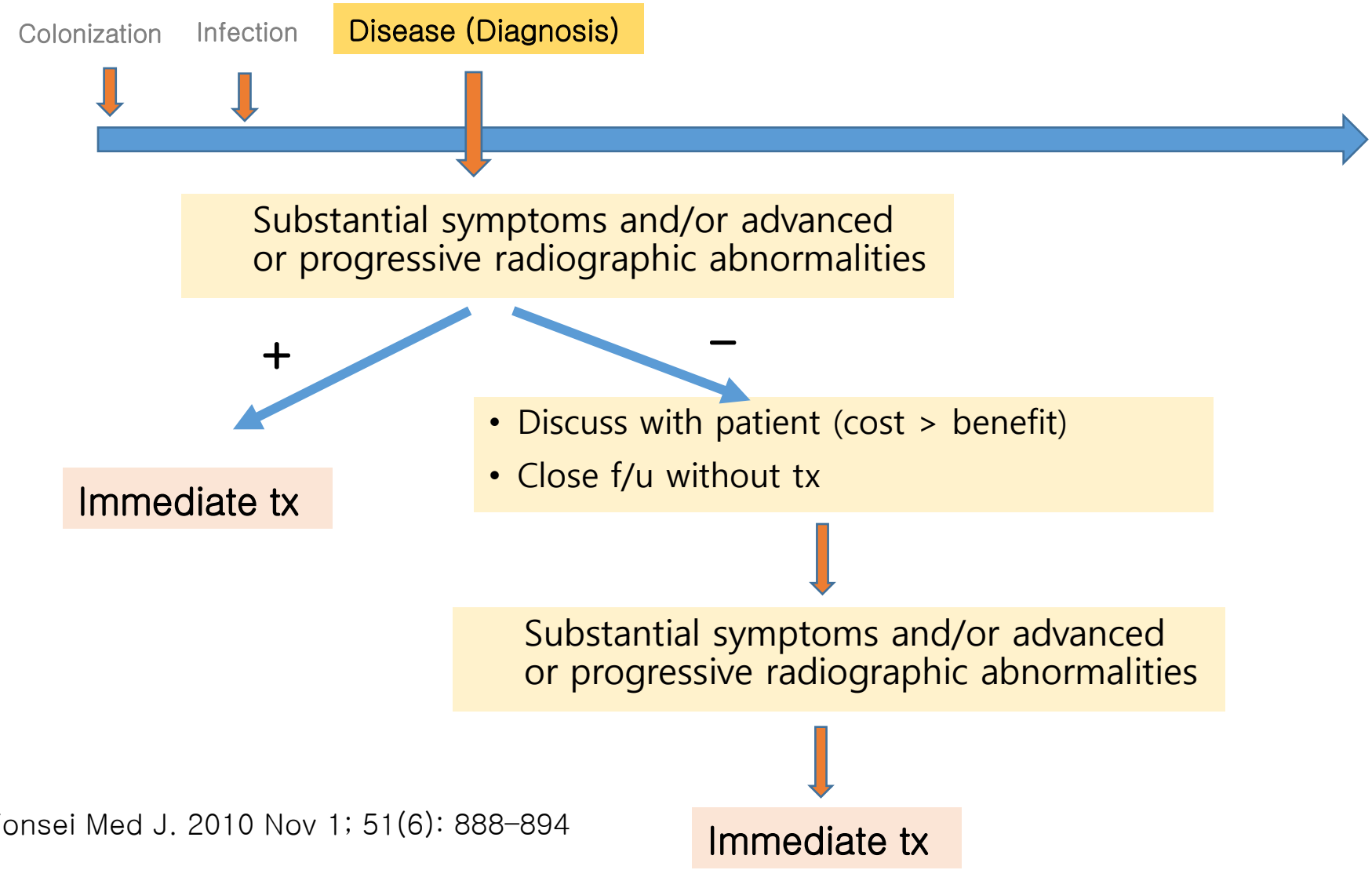
- Sputum culture conversion (> 3 culture neg, > 3 mo) :86%
  - Microbiologic recurrence(MR) during therapy : 14%
    - **Reinfection : 73%, Relapse : 27%**
- Treatment success (sputum conversion without relapse) : 84%
  - MR after completion of therapy : 48%
    - **Reinfection : 75%. Relapse : 25%**

Chest. 2014 Aug; 146(2): 276–282

Cost of MAC lung disease (early treatment)

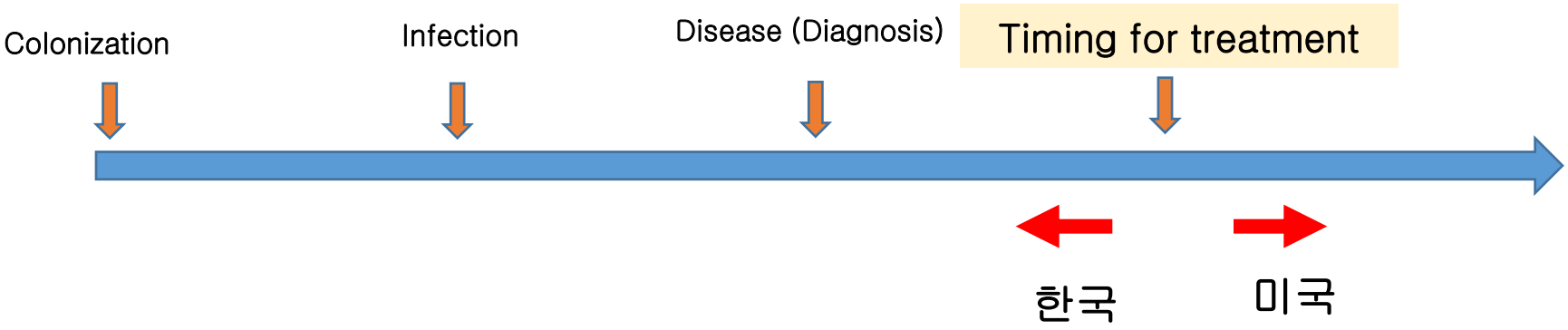
- Difficult to tx
  - Long duration of tx (> 18 mo)
  - High cost
    - 약 값 (clarithromycin, rifampin, ethambutol, streptomycin) 18 mo
    - 검사비 , 교통비, 인건비...
  - Adverse drug reactions
- Development of drug resistance

Treatment of MAC lung Disease



Yonsei Med J. 2010 Nov 1; 51(6): 888–894

Decision of timing for treatment of MAC lung Disease



- Difficult to tx
  - Long duration of tx (> 18 mo)
  - High cost
  - Adverse drug reactions
- Development of drug resistance

환자의 치료 의지

- Improve symptoms
- Preserve lung function
- Bacteriologic Response to tx (bacterial conversion, reinfection..)

Timing of MAC lung disease treatment

Delay until the Benefit exceeds Cost

경청해 주셔서 감사합니다