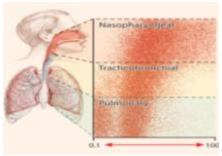
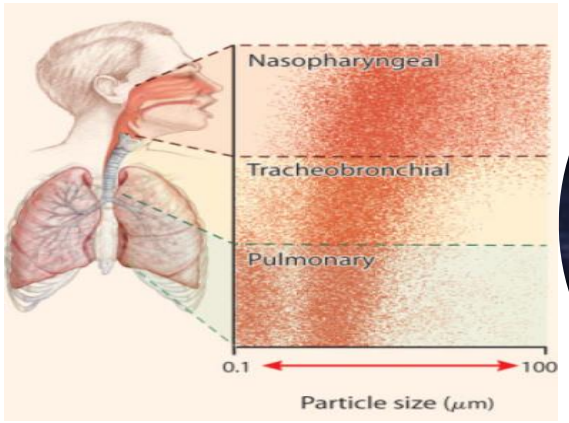
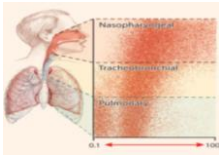


결핵의 감염 및 잠복결핵



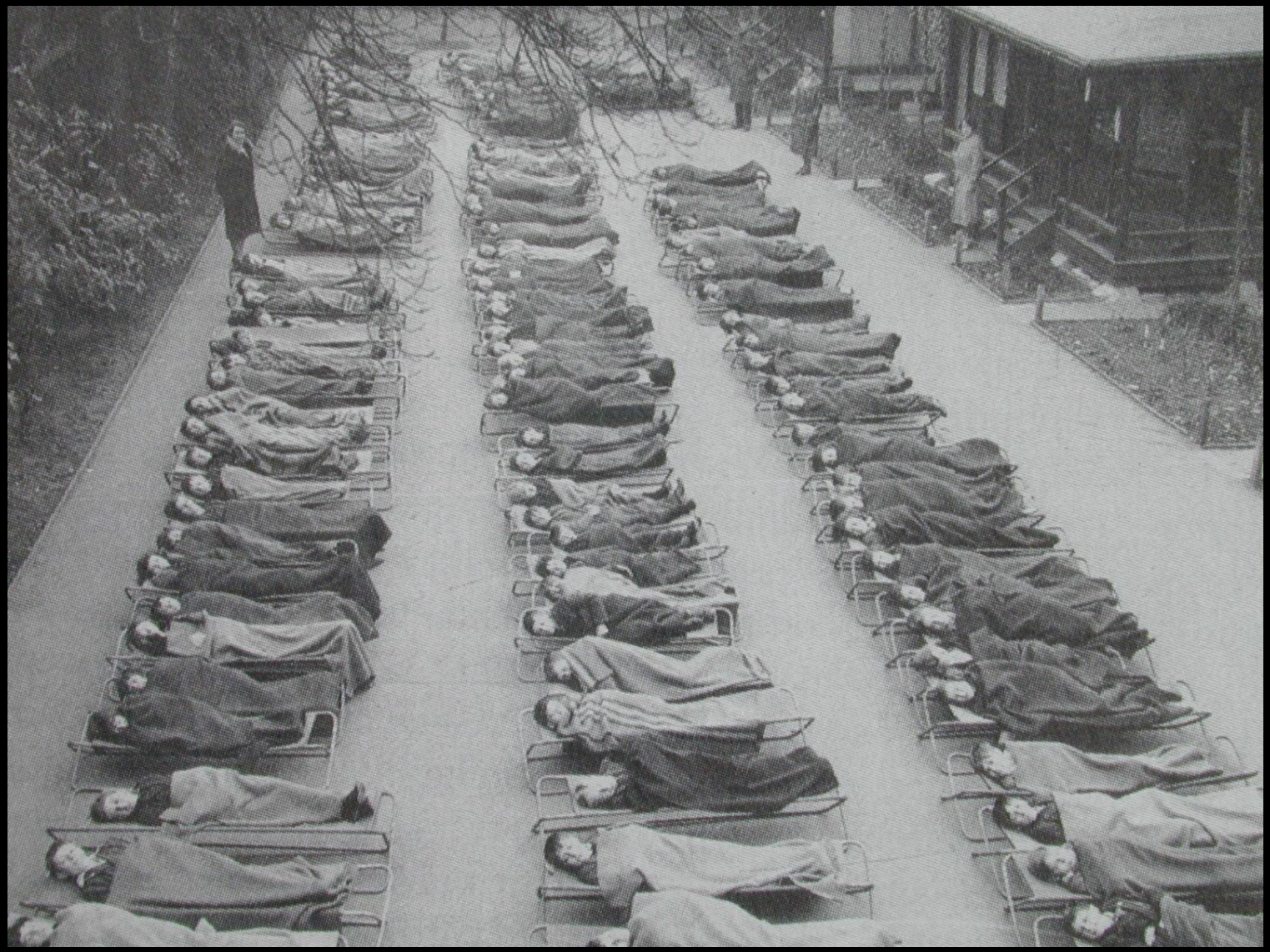
2016. 11. 13
고려대학교 안산병원 호흡기내과
이승헌



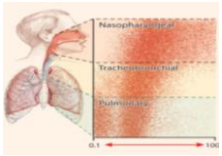
목차

- 서론
- 결핵균의 전염기전
- Riley의 결핵균 전염 실험 및 모델
- 임상적 측면에서의 결핵환자의 전염성
- 접촉자의 결핵 감염 및 결핵 발병 위험성
- 결핵의 전염 차단 및 감염관리 지침
- 결핵의 진행 및 잠복결핵 감염 치료
- 결론

Children with Tuberculosis at Springfield House Open Air School, Clapham Common, London, United Kingdom, November 1932



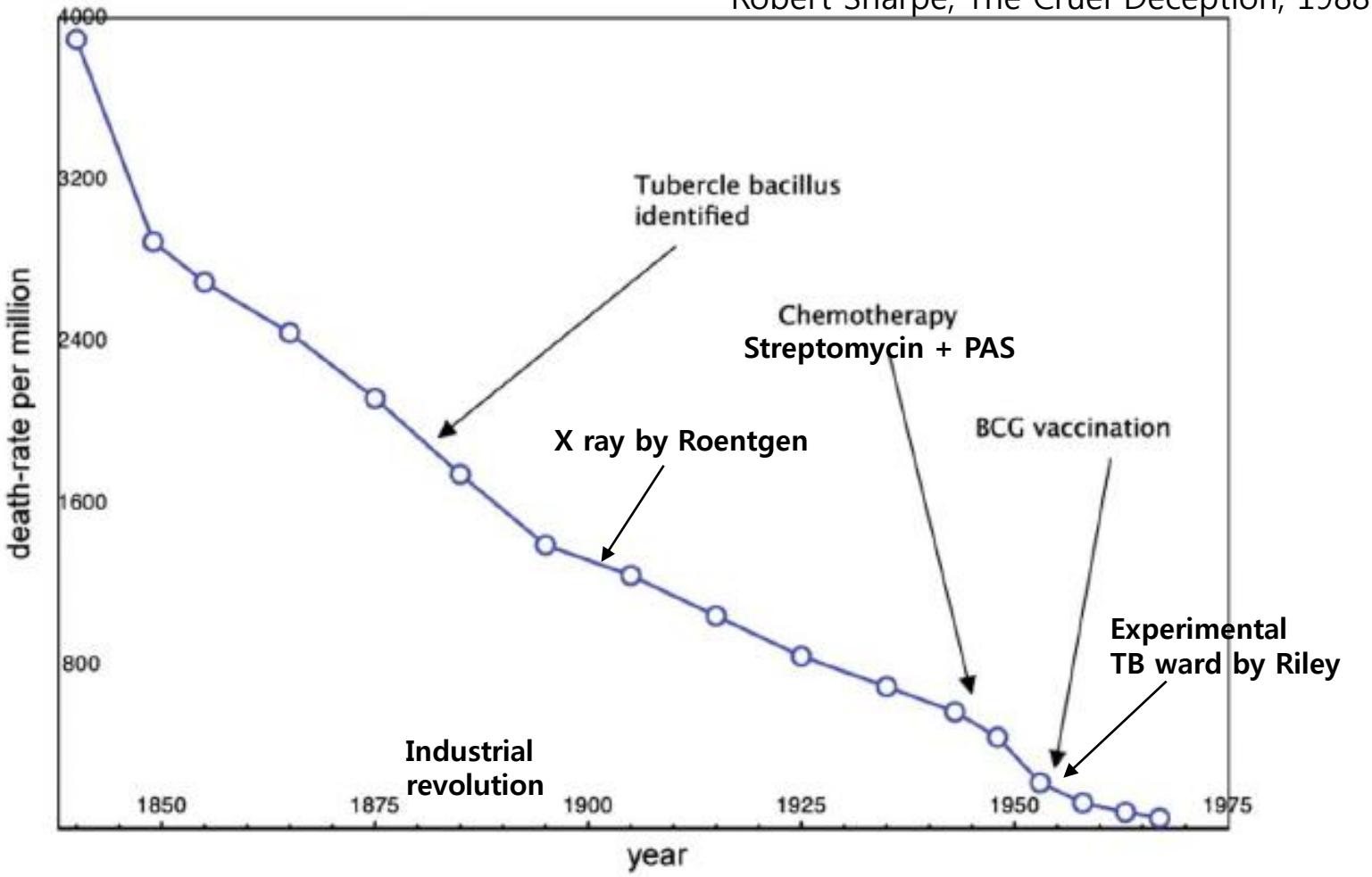
Jacobson C. Lancet 2001;358:340
Photo: Hutton Getty

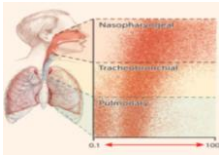


TB death rate and chronology

Respiratory TB death-rates in England and Wales

Robert Sharpe, The Cruel Deception, 1988





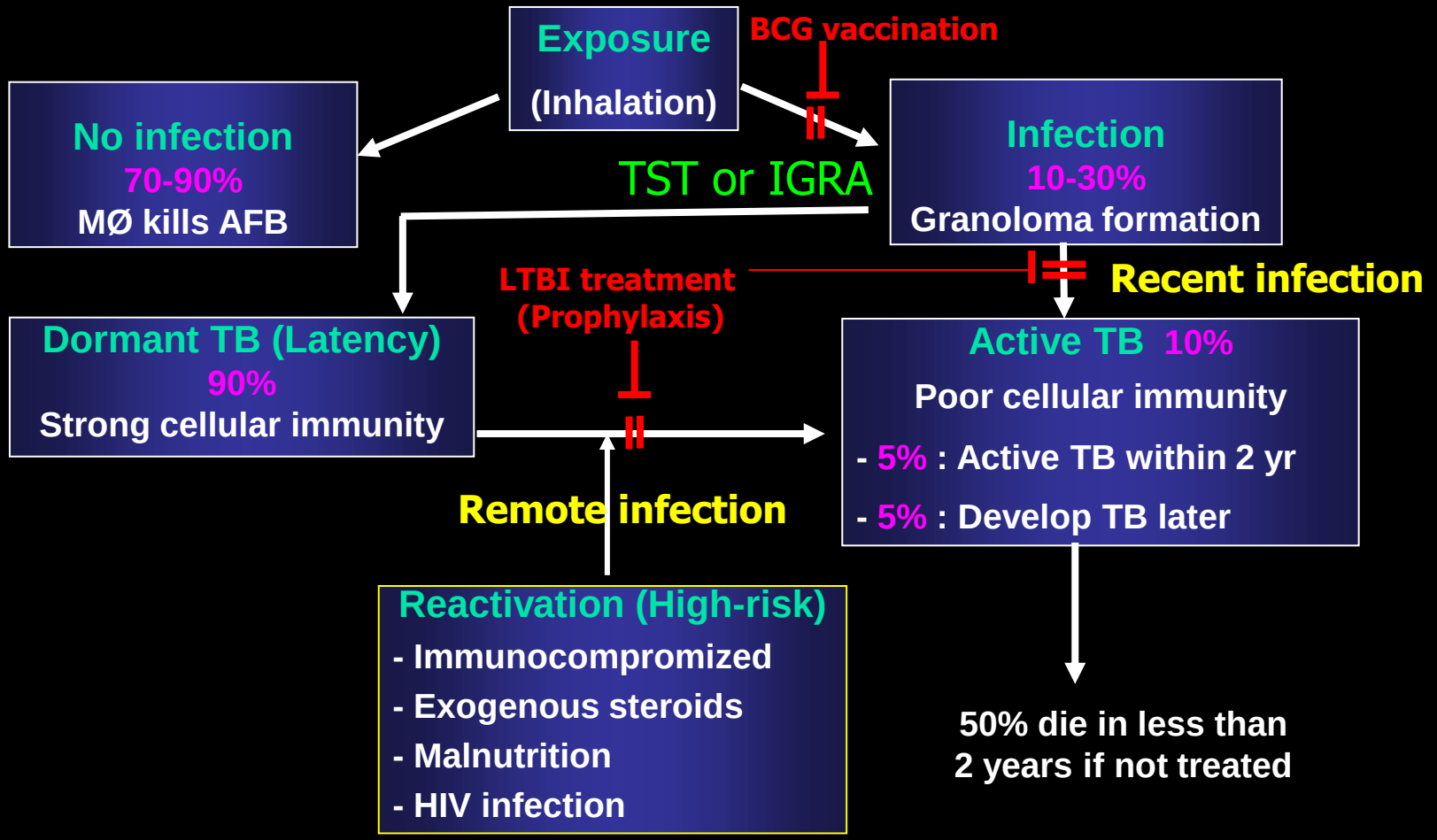
서론

- 공기매개감염
- 잠복결핵감염: 세계 인구의 1/3감염
- 잠복결핵 유병률: 저소득 및 중간소득국가 51.5%, 고소득국가 28.1%
- 결핵관리정책:

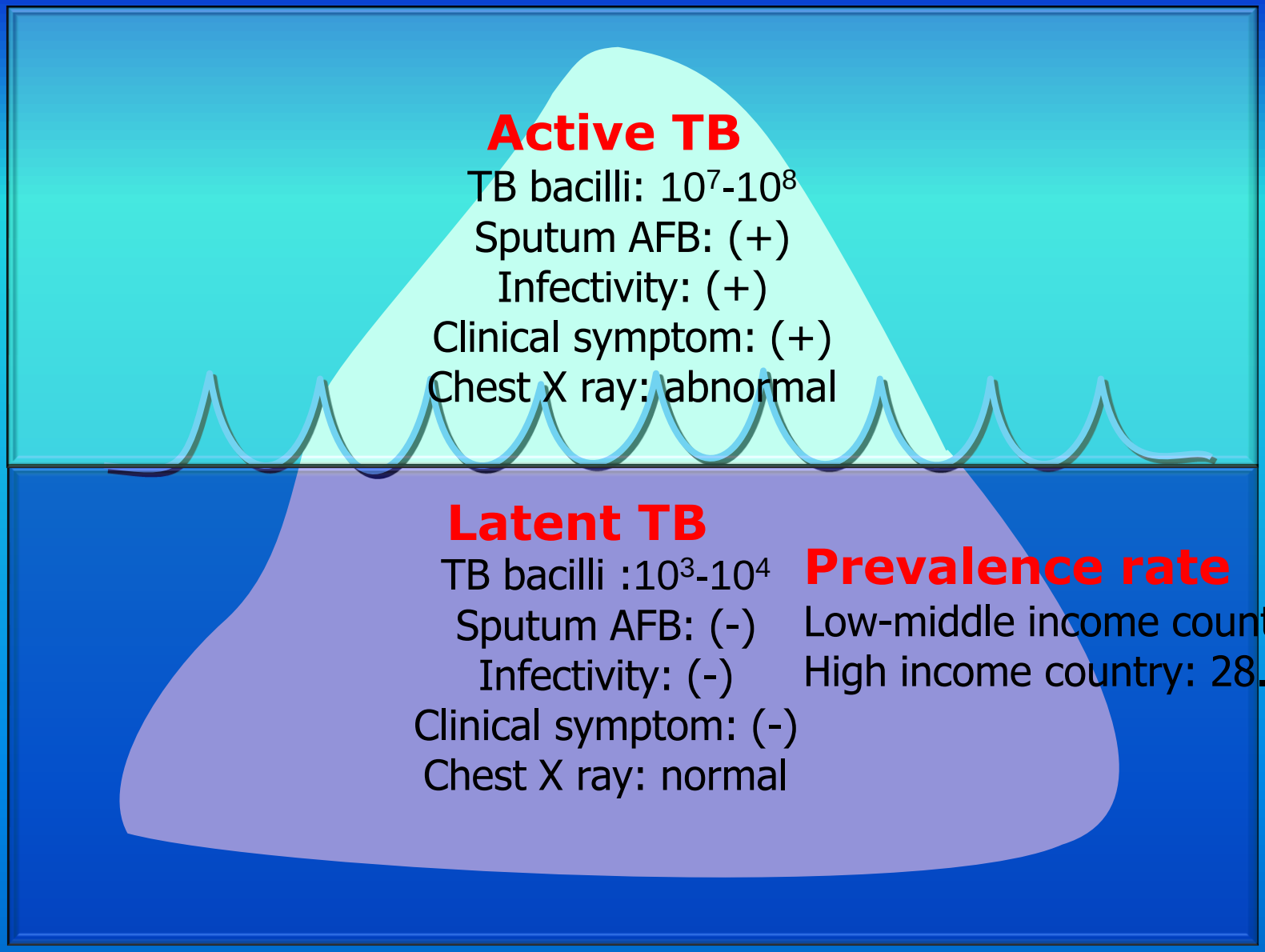
-결핵 고위험율 국가: BCG vaccine/활동성결핵환자 발견 사업(active, passive)

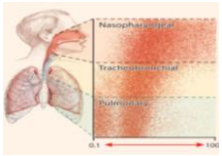
-결핵 저위험율 국가: 잠복결핵치료, 이주민 관리

Natural history of TB



Sutherland I. Adv Tuberc Res 1976;19:1-63.


Active TB
TB bacilli: 10^7-10^8
Sputum AFB: (+)
Infectivity: (+)
Clinical symptom: (+)
Chest X ray: abnormal
Latent TB
TB bacilli :10^3-10^4
Sputum AFB: (-)
Infectivity: (-)
Clinical symptom: (-)
Chest X ray: normal
Prevalence rate
Low-middle income country: 51.5%
High income country: 28.1%



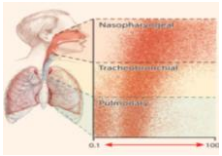
Transmission by aerosols

- The agent's capacity to be transmitted
- To induce disease through fine-particle aerosols and other routes.

  -Obligate: TB- initiated only through aerosols, depositived in the distal lung.

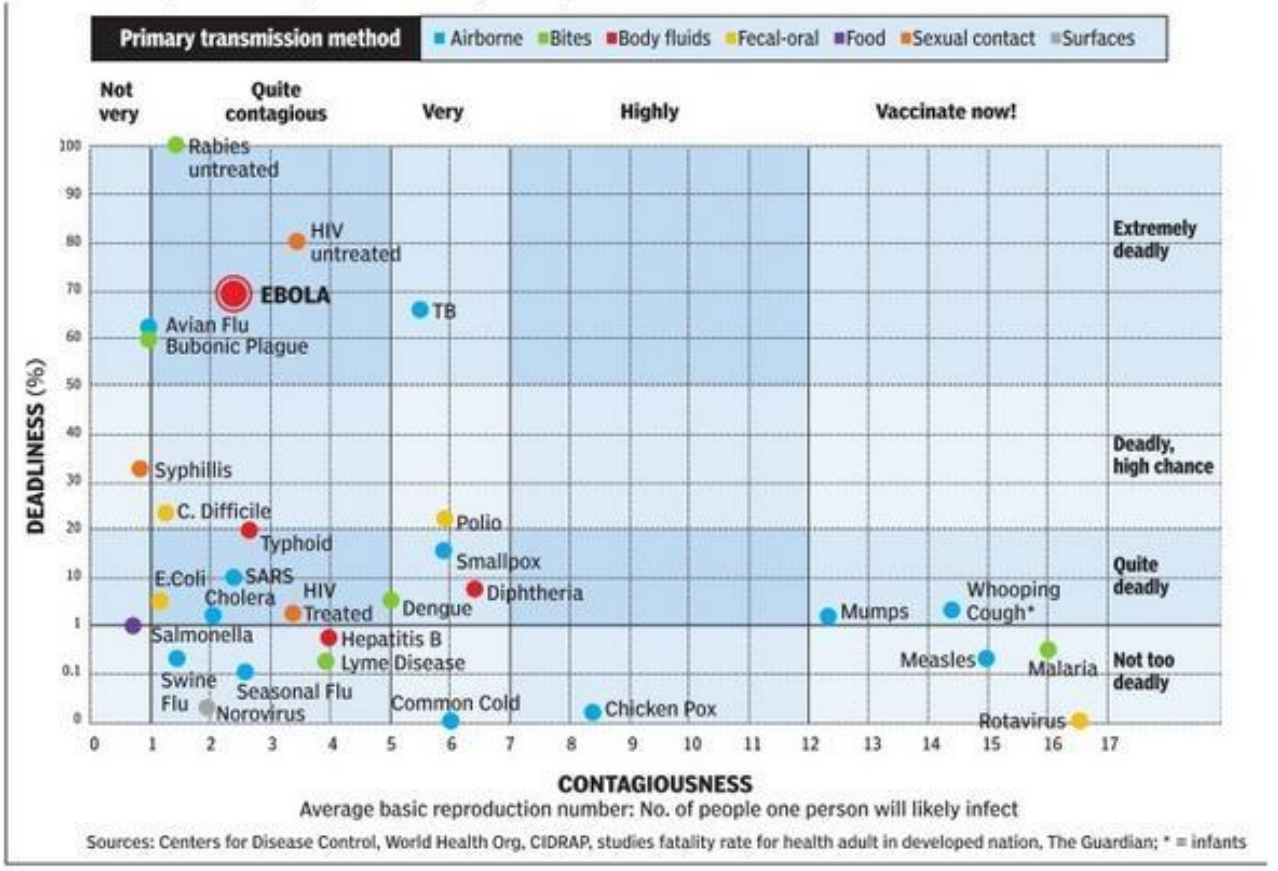
  -Preferential: can naturally initiate infection through multiple routes but are predominantly transmitted by aerosols deposited in distal airways; with these agents, infection initiated through another route usually causes modified disease

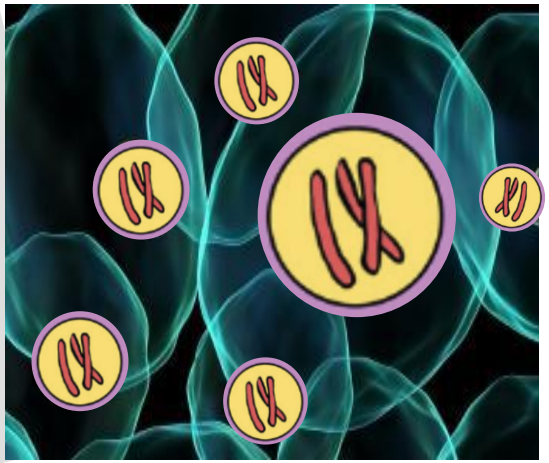
  -Opportunistic



Basic Reproductive Rate (Ro)

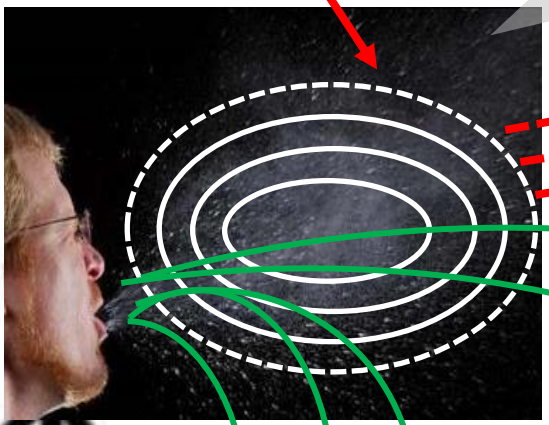
- The average number of persons infected by a single disease source.





Small droplets evaporate to Droplet nuclei in this zone

Ventilation



Droplet nuclei
(< 5 μm, 1-10 TB bacilli)
Carried in air currents
for minutes to hours

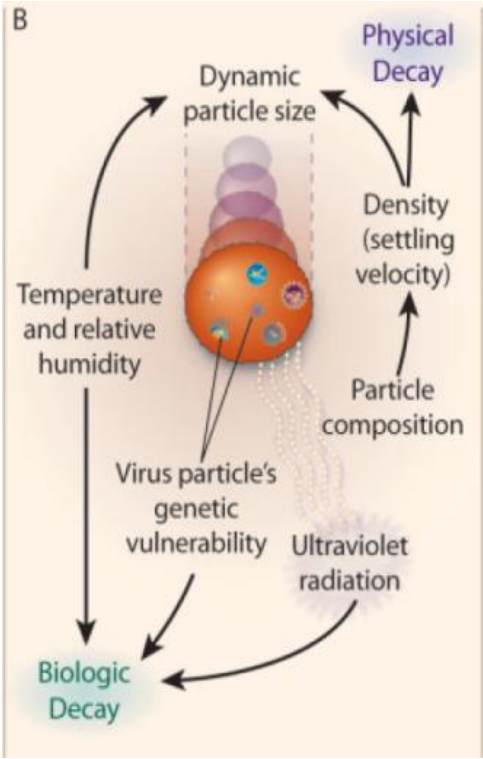
Respiratory droplet
(> 100 μm)

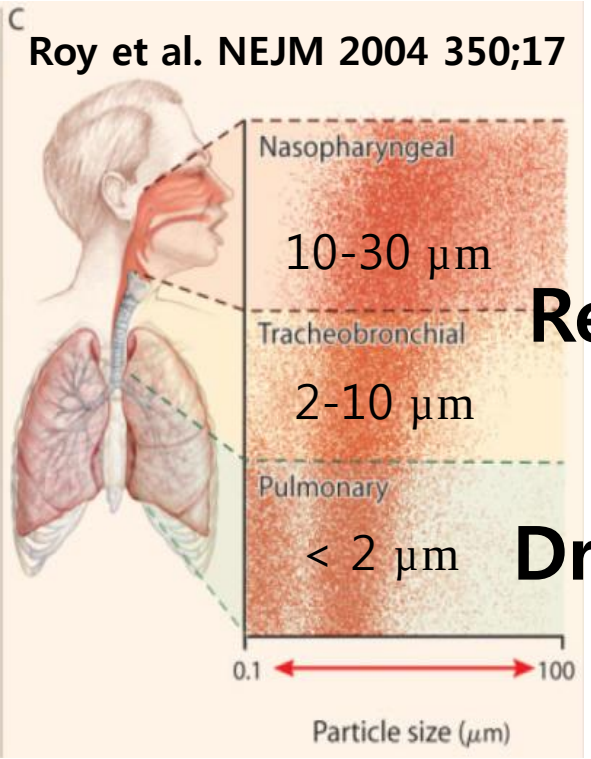
1m

4m

Droplet from activities & transmission pathway

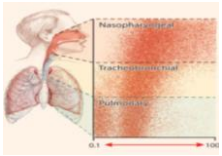
Activity	Approximate particle count	Units
Sneezing [36]	40,000	Per sneeze
Bowel evacuation [37]	20,000	Per event
Vomiting [38]	1,000	Per event
Coughing [36]	710	Per cough
Talking [36]	36	Per 100 words





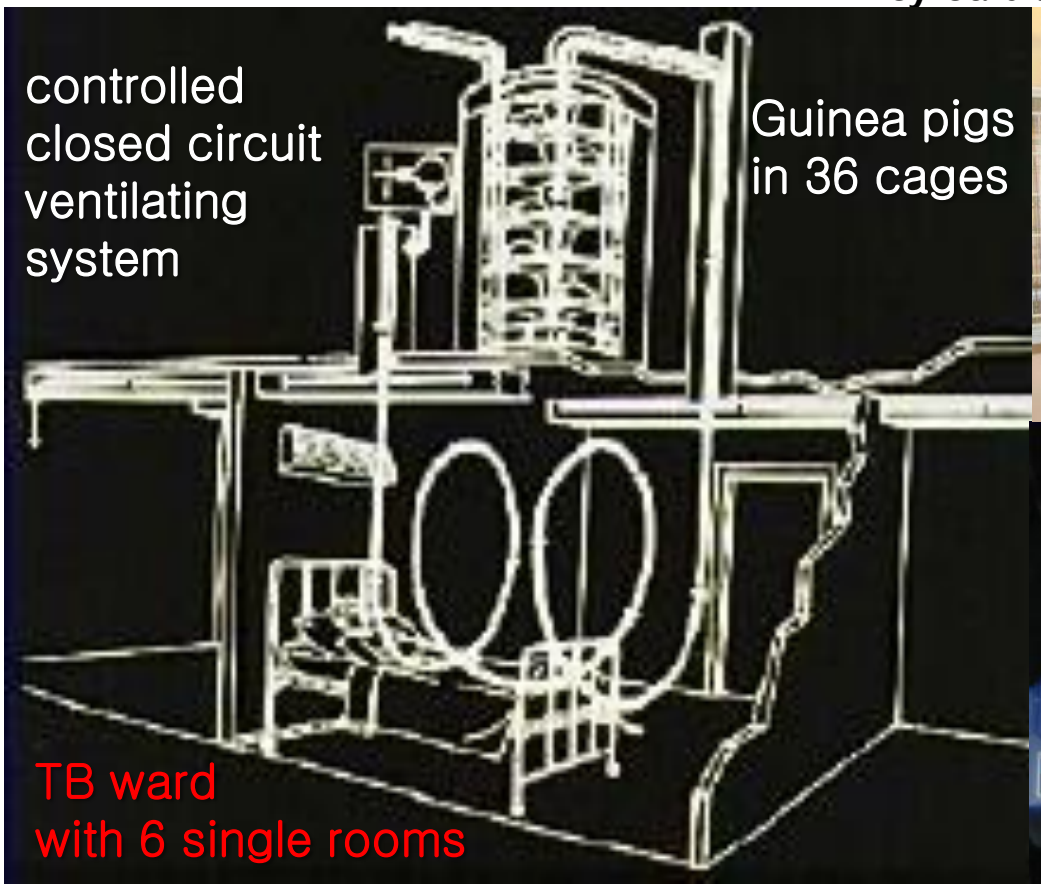
Respiratory droplet

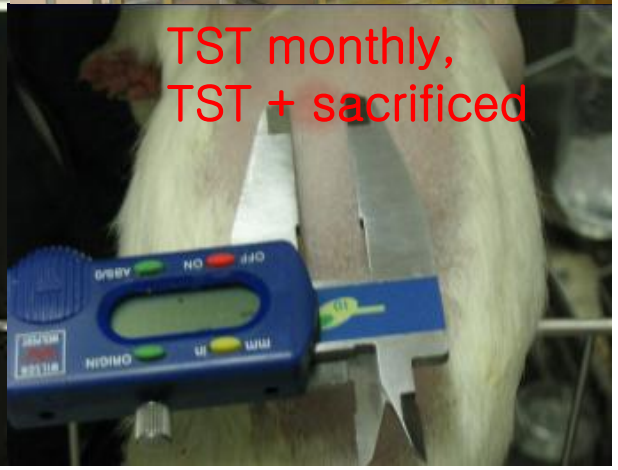
Droplet nuclei



Experimental TB ward 1956.11~1958. 11

Riley et. al. Am. J. Hyg. 1959; 70: 185-196





- Sputum + patients/month in the ward: 3.5~6 patients
- Guinea pigs exposed at one time: 74–187 guinea pigs (average 156)
- Ward air: distributed radially through the cages before being vented

Initial treatment for drug susceptible TB patients

Drug resistant organisms Were placed on the ward

Table 1. Occupancy of exposure chamber and fate of animals exposed

year----------	1956					1957												1958										
Month----------	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
Sacnifced																													
Tuberculosis					2	3	1	7	4	5	5					1	1		2	8	2	1	3	5	2	2	10	6	1
Tuberculin reaction																													
≤10mm diam.																													
< 3+ induration																													
No central necrosis								4	3		1		2		1	1						1	2			2	1		
Pasteurella																													
Multiple abscesses					2		2	3	7		9		6																
Well animals																													
Natural deaths																					3	4					34		
Pneumonia																													
Acute											1													3		25	5		
Chronic Mostly due to																													
Pasteurella		6	11	3	4	3		1	3	10	2	2	2	3	4				2	1	2	6	1	6	5	2			
Other infections, mostly																													
peritonitis					1			2			2																		
Trauma	3				2	2		1	1	1			1	1	1		1			3		2	2		2	3			
Removed alive for observations			7													4		5			1			1		4			
Unaccounted for	2	3	5						1	1			1	1	1		2		2	1	1	1	2	1	3				
Total removed	5	9	23	3	11	8	3	18	19	17	20	2	12	5	7	6	4	5	6	13	9	15	10	16	12	38	51	7	1
New animals added	37	35			81	3	41	19	10	2	22	14	1	35			11		2	19		28	2		7			4	
Change in occupancy	32	26	-23	-3	70	-5	38	1	-9	-15	2	12	-11	30	-7	-6	7	-5	-4	6	-9	13	-8	-16	-5	-38	-51	-3	
Total Occupancy at end of indicated month	73	99	76	73	143	138	176	177	168	153	155	167	156	186	179	173	180	175	171	144	168	181	173	157	152	114	63	60	
Average occupancy for indicated month	68	70	89	74	115	138	165	175	168	158	150	161	159	179	181	171	177	175	172	164	171	187	174	163	154	131	86	61	

Riley et. al. Am. J. Hyg. 1959; 70: 185-196

- A total of 373 new animals between 1956.11.1~ 1958.11.1
- Great variation in the infectivity for guinea pigs of aerosolized sputum from different patients

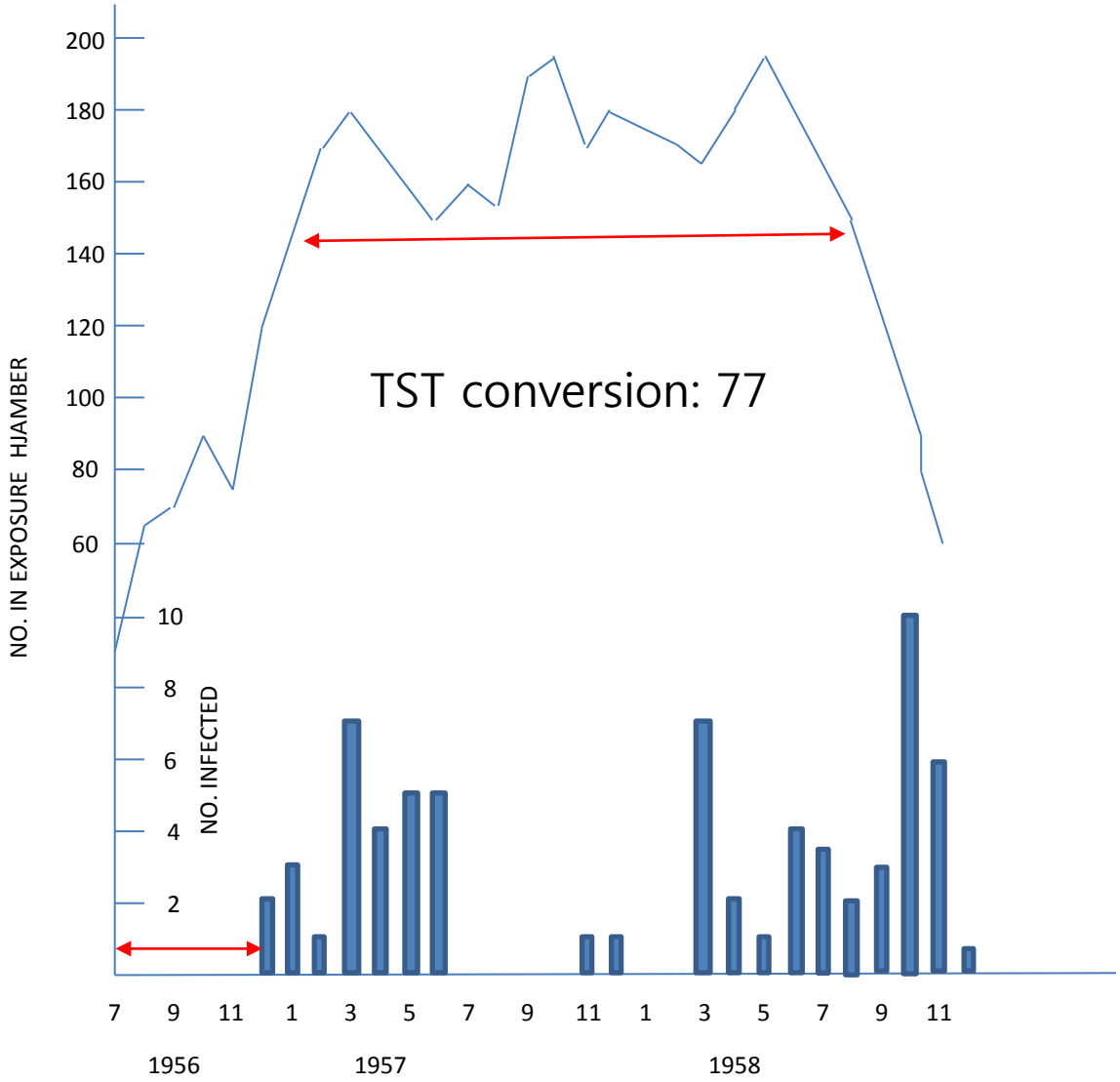


Figure 1.
Average number of guinea pigs in exposure chamber each month and number identified as having tuberculosis each month.

Riley et. al. Am. J. Hyg. 1959; 70: 185-196

X	X X	XXX	X X	X X X X	X X
X	X	XXX	X X	X	X
X	X	X X X	X X		
X X X X X	X	X			XXX
X	X X	X	XXX XXX	X X	XXX
X X	X	X X	X X	X X	X X

Figure 2. Distribution of TB infections by cages. The frame holding the 36 cages rotates, so each cage maintained a constant position relative to the others. All 71 infections are included.

Table 2. Pathological findings in guinea pigs sacrificed because of TST conversion

No.	Date	Pulm. tubercles: NO.	Pulm. tubercles: Position	Bacilli seen in*: Hilar nodes	Bacilli seen in*: Spleen	Remarks
	1956					
1	12/4	1	R.L.L.			
2	12/5	1	R.L.L.			
	1957					
3	1/2	1	L.U.L.			Patient : Art *R to SM, INH, PAS
4	1/2	0		+		
5	1/2	1	R.U.L.	+		
6	1/28	1	R.L.L.	+		
7	2/25	1	R.U.L.	+		
8	2/25	1	R.U.L.	+		
9	2/25	1	R.U.L.	+		
10	2/25	0		-		No tbc
31	8/5	0		-		No tbc
32	10/30	1	R.L.L.	+	-	
33	10/30	0		+		No tbc
34	11/25	0		+		Patient : Jon *R to SM, PAS
	1958					
35	2/3	0		+	+	
36	2/3	1	L.U.L.	+	+	
37	3/3	0		+	+	
38	3/3	0		+	+	
39	3/3	2	R.U.L.	+	+	1 tubercle larger

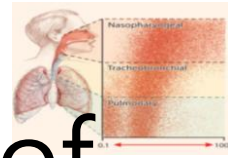
NO.	Date	Pulm. tubercles: No.	Pulm. tubercles: Position	Bacilli seen in*: Hilar nodes	Bacilli seen in*: Spleen	Remarks
40	3/3	1+	L.U.L.	+	+	Secondary spread
41	3/3	0		+	+	
42	3/3	1	R.U.L.	+	-	
43	3/3	1	L.L.L.	+	+	
44†	2/19	1	L.U.L.			Natural death
45	3/31	1+	R.U.L.	+	+	Secondary spread
46	3/31	1	L.U.L.	+	+	
47	4/28	2	L.L.L.	+	+	Tubercles Conti-guous
48	5/27	1‡	R.L.L.	+	+	
67	9/23	0		+	+	
68	9/23	0		+	+	
69	9/23	1+	L.U.L.	+	+	Secondary spread
70	9/23	1	L.U.L.	+	+	
71	10/15	1+	L.L.L.	+	+	Secondary spread
72	10/15	1	R.L.L.	+	+	
73	10/15	1‡	L.U.L.	+	+	
74	10/15	1‡	L.U.L.	+	-	
75	10/15	0		+	+	
76	11/10	1	R.U.L.	+	+	
77	12/10	1	R.L.L.	+	+	

TB infection: 71 / 77
-pul. Tubercle: 51
-hilar node+: 20

Tubercle number in guinea pigs exposed simultaneously was almost same
:tubercles number depends on the number of infectious droplet nuclei inhaled

Riley et. al. Am. J. Hyg. 1959; 70: 185-196

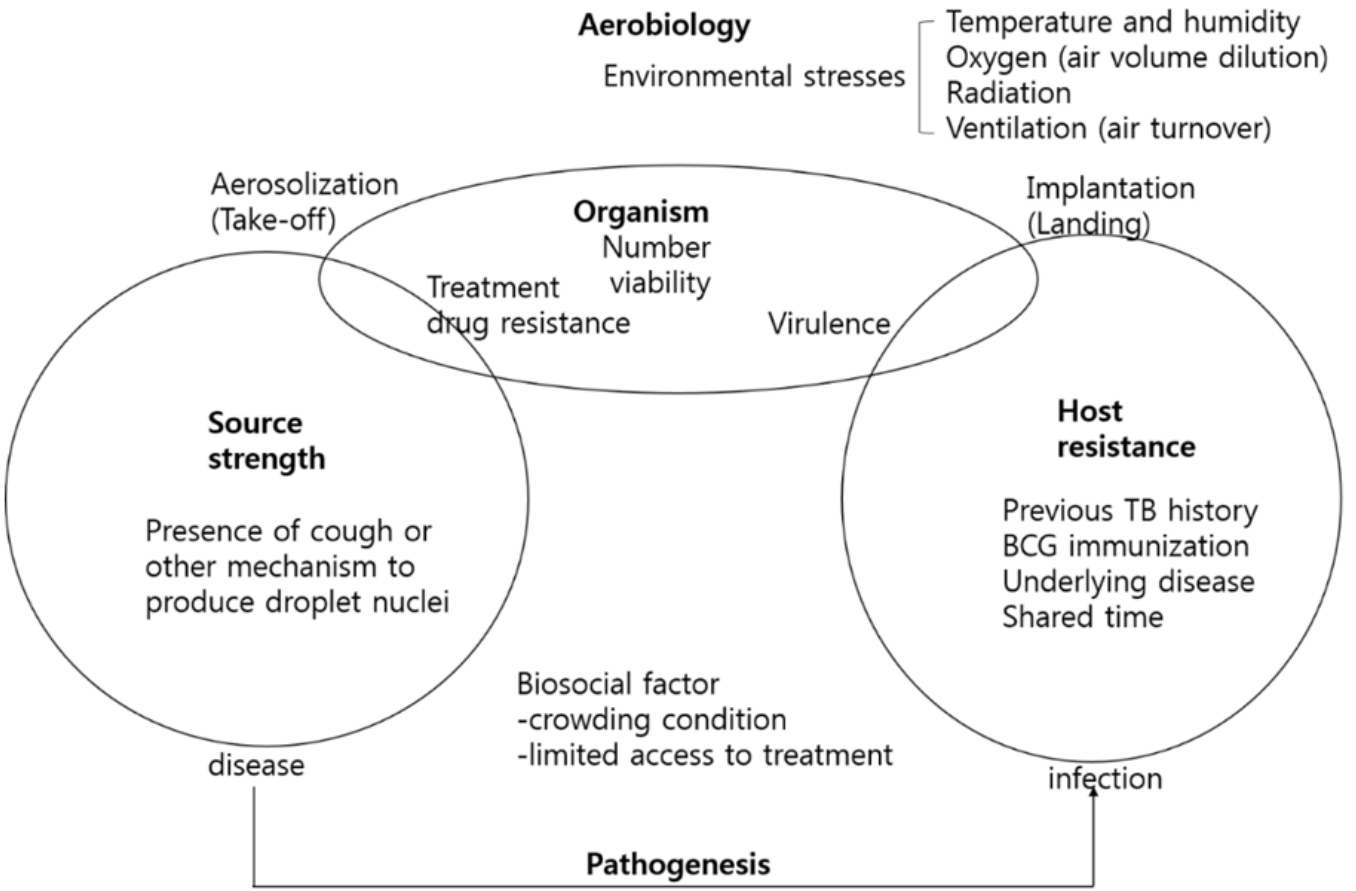
*A blank indicates that the tissue was not examined histologically.
†Tuberculin trst ± snice 3/26/57. ‡NO tuberculosis seen histologically in pulmonary tubercle.



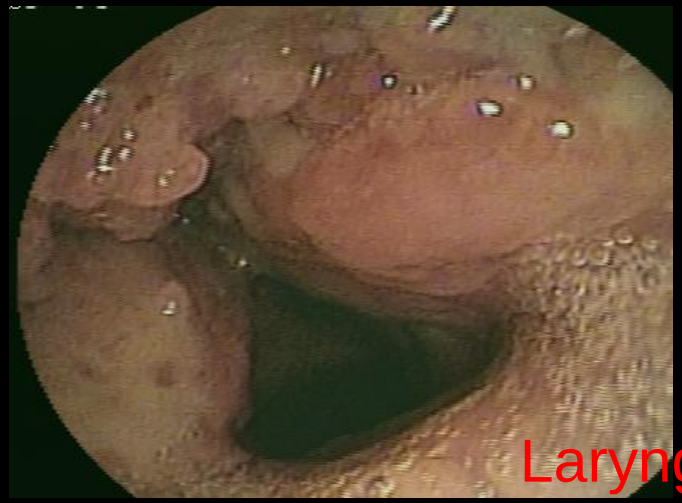
Factors determining the likelihood of transmitting TB infection.

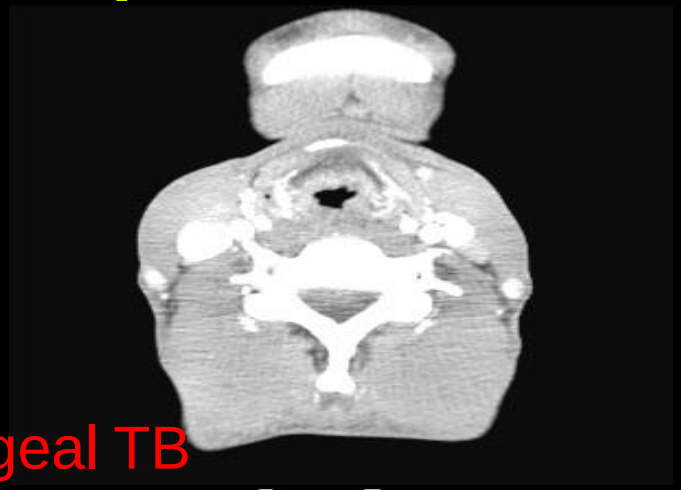
$C = S\,(1-e^{-Iqpt/Q})$

C = number of new cases
S = number of susceptibles exposed,
e = natural logarithm
I = number of infectious sources
q = number of quanta (infectious doses) generated
per unit min
p = human ventilation rate (L/min),
t = exposure duration
Q = infection-free ventilation (L/sec)
(Assumption: uniform susceptibility of exposed persons to
infection, uniform virulence of organisms from one outbreak
to another.)



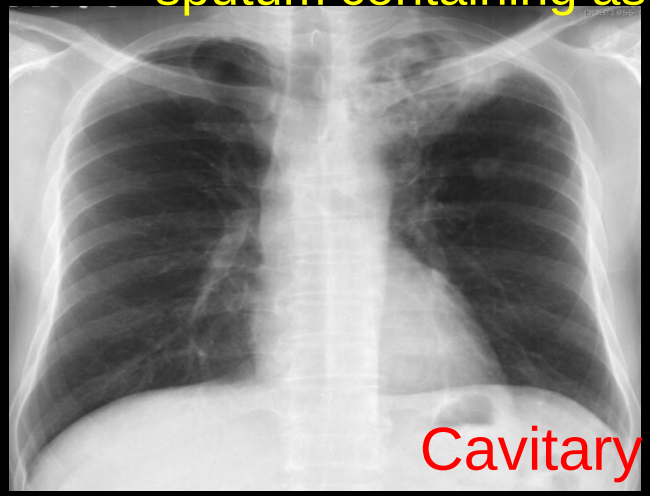
Infectious patients

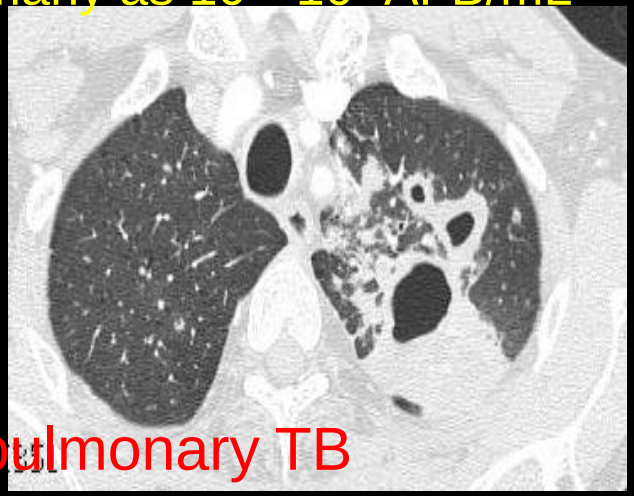




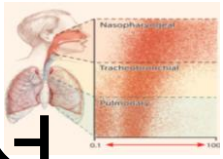
Laryngeal TB

sputum containing as many as 10^5–10^7 AFB/mL





Cavitary pulmonary TB

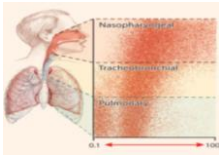


임상적 측면에서 결핵환자 전염성

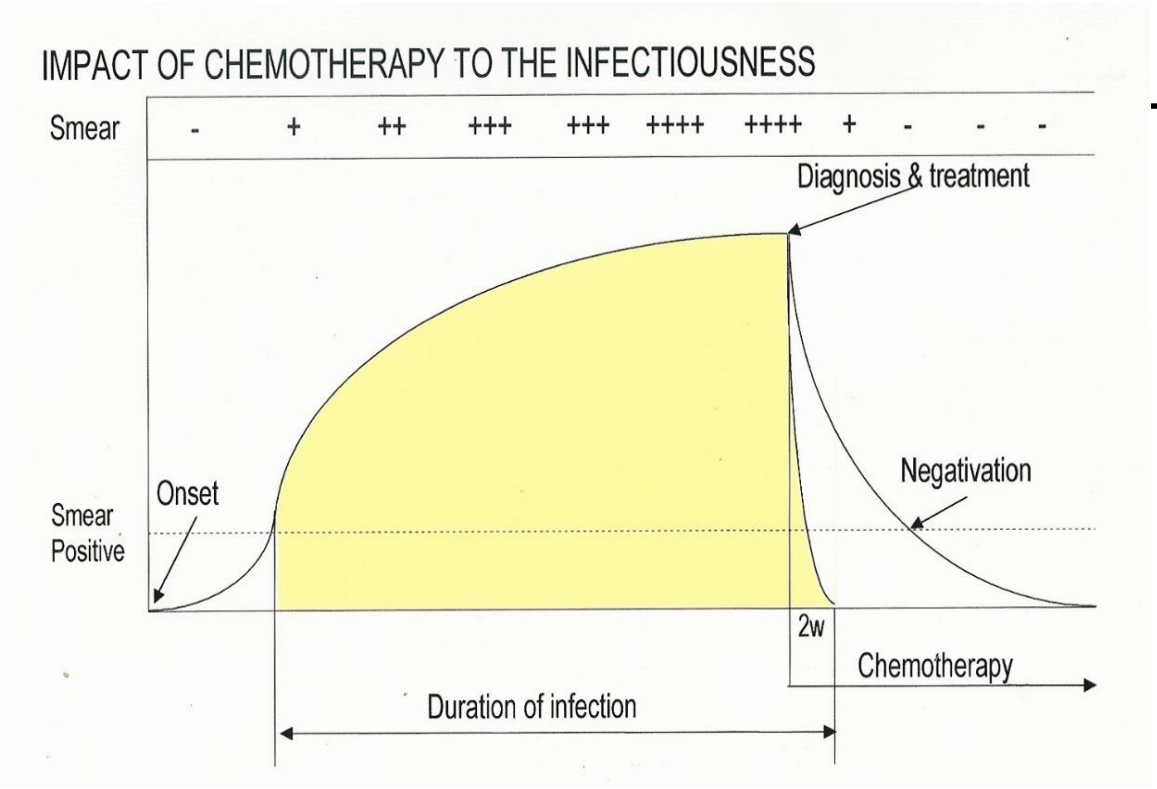
Table 2. Guidelines for estimating the beginning of the period of infectiousness of persons with TB, by index characteristics[17].

Characteristic			
TB symptoms	AFB* sputum smear positive	Cavitary chest radiograph	Recommended minimum beginning of likely period of infectiousness
Yes	No	No	3 months before symptom onset or first positive finding (e.g., abnormal chest radiograph) consistent with TB disease, whichever is longer
Yes	Yes	Yes	3 months before symptom onset or first positive finding consistent with TB disease, whichever is longer
No	No	No	4 weeks before date of suspected diagnosis
No	Yes	Yes	3 months before first positive finding consistent with TB

SOURCE: California Department of Health Services Tuberculosis Control Branch; California Tuberculosis Controllers Association. Contact investigation guidelines. Berkeley, CA: California Department of Health Services; 1998.
* Acid-fast bacilli.



결핵약물 치료로 인한 감염성의 감소



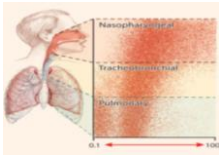
The viable units ↓

-1/20 within 2 days

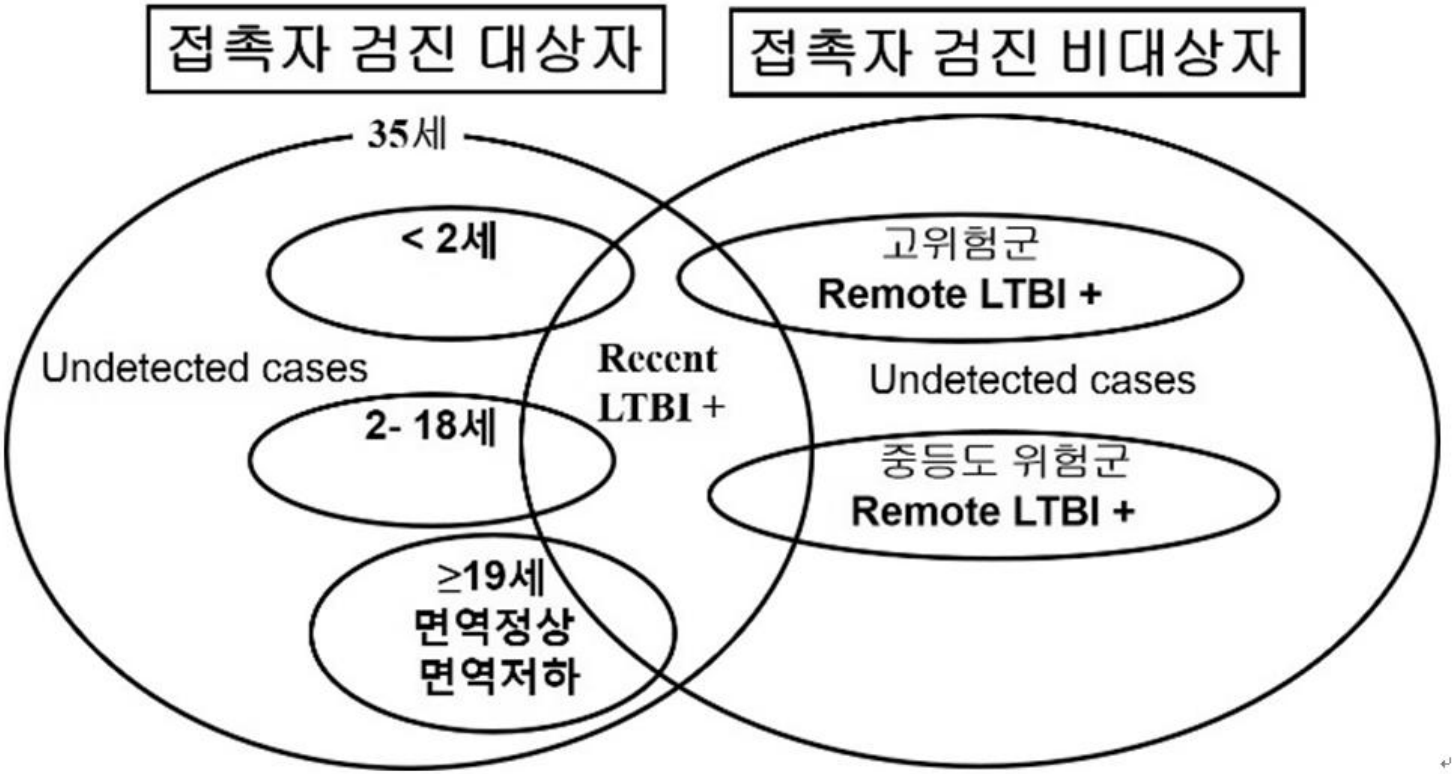
-1/200 within 14 days

-fall to 10^5/ml within the first 2 weeks

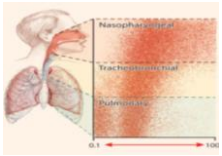
(Jindani A et al, 1980)



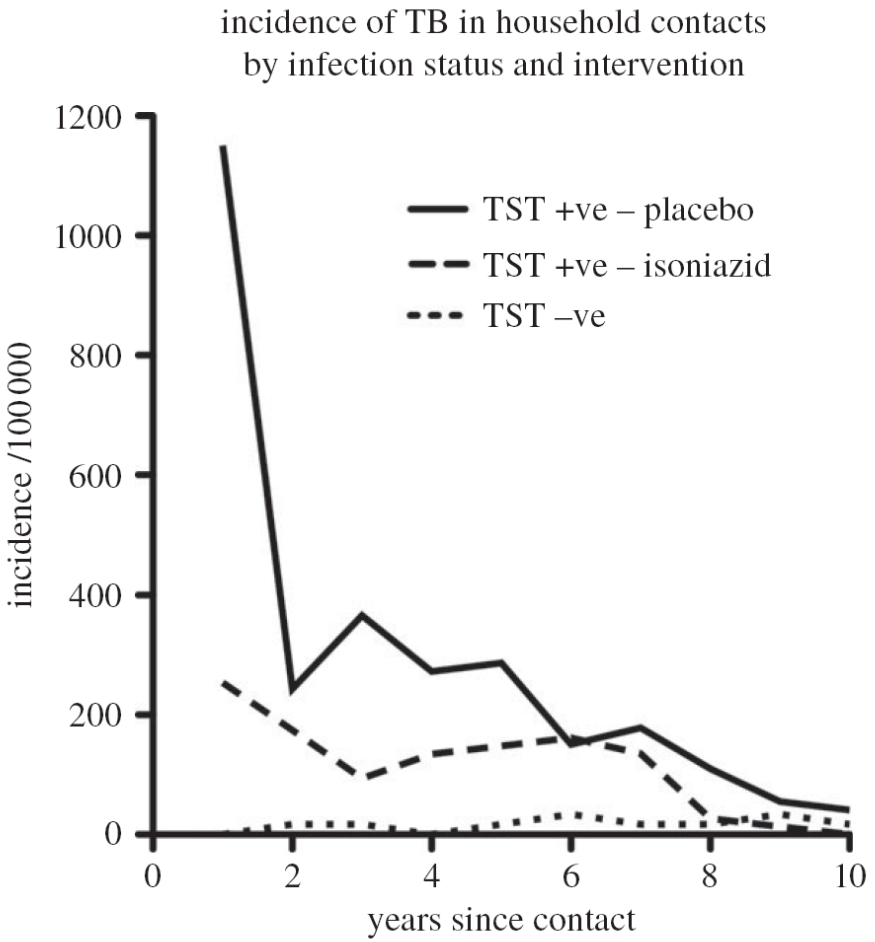
접촉자의 결핵 감염



A schematic diagram for LTBI (latent TB infection) screening in TB contacts and non-TB contacts in Korea

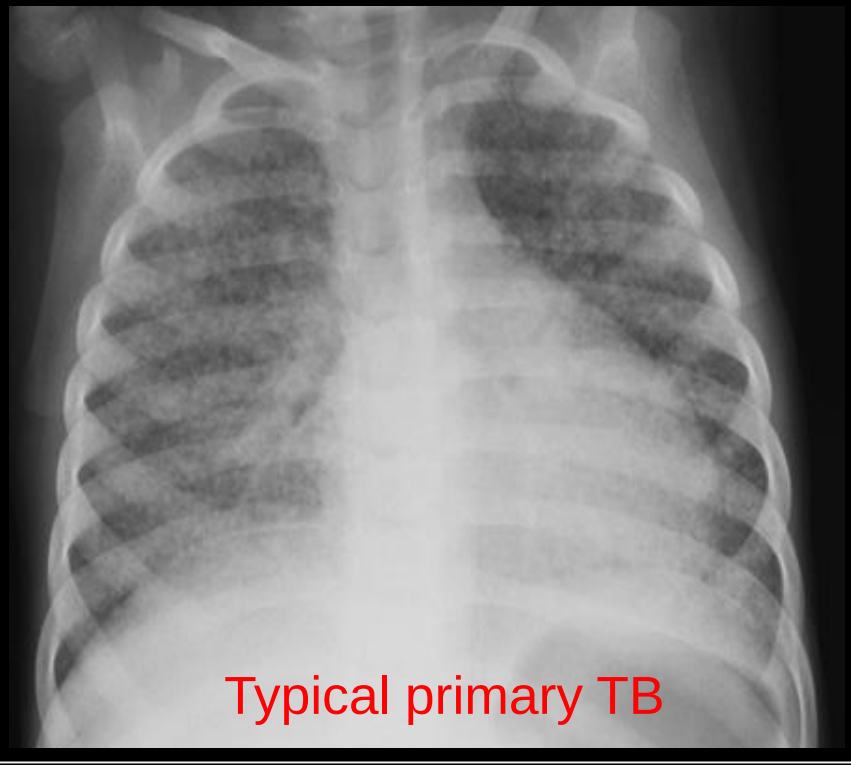


Reactivation from LTBI



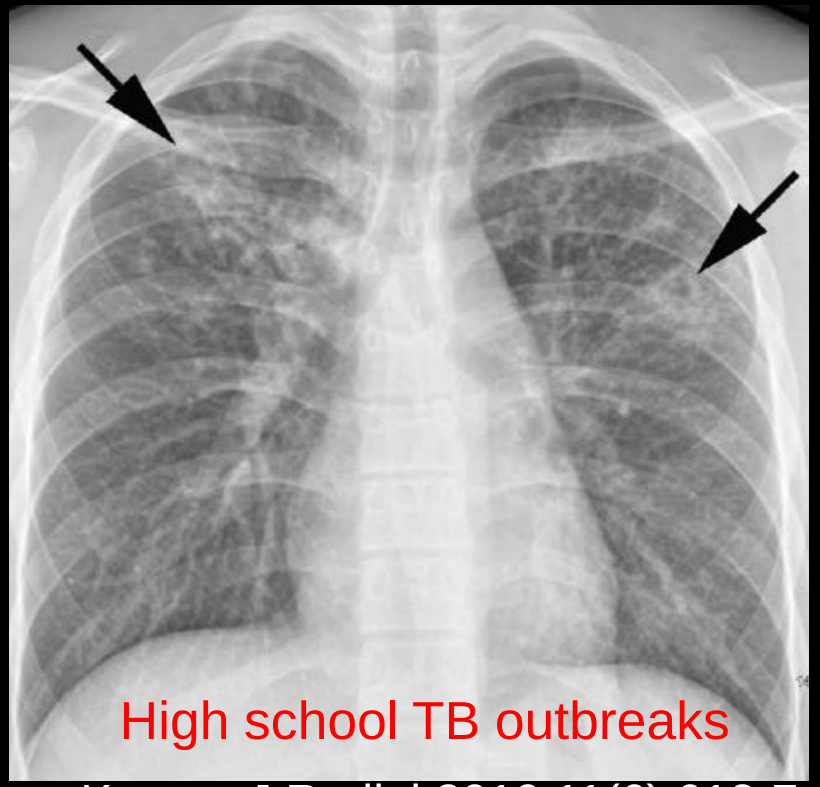
Esmail et al. Philos Trans R 2014 May 12;369:1645

-most within the first year following infection
-stepwise reduction over the following 5–10 years



Typical primary TB

- -Middle and lower lung zones
- -Mediastinal lymphadenopathy
- -May be disseminated
- -Can be healed spontaneously

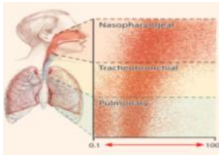


High school TB outbreaks

Korean J Radiol 2010;11(6):612-7

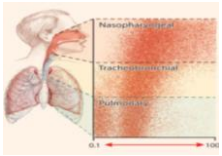
Male/ 18 year-old boy
with typical radiographic findings
mimicking reactivated TB

Distinction has been challenged by molecular evidence
:a large percentage of cases of adult pulmonary TB result from recent infection (either primary infection or reinfection) and not from reactivation.



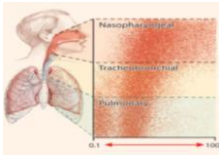
Infection control :Health-care facilities

Scopes of infection controls	Contents
Health-care facilities	
Managerial activities	Identify and strengthen a coordinating body for TB infection control: Political commitment, and setting of leadership Developing a facility plan (budget, human resources, spaces, policies, and procedures) On-site surveillance of TB, address advocacy, communication and social mobilization (ACSM), monitor and evaluation/research
Administrative controls	Identification (triage) and separation of TB suspects Minimizing the time spent in facilities Package of prevention and care interventions
Environmental controls	Reducing the concentration of infectious respiratory aerosols Controlling the direction of infectious air
Personal protective equipment	Particulate respirators

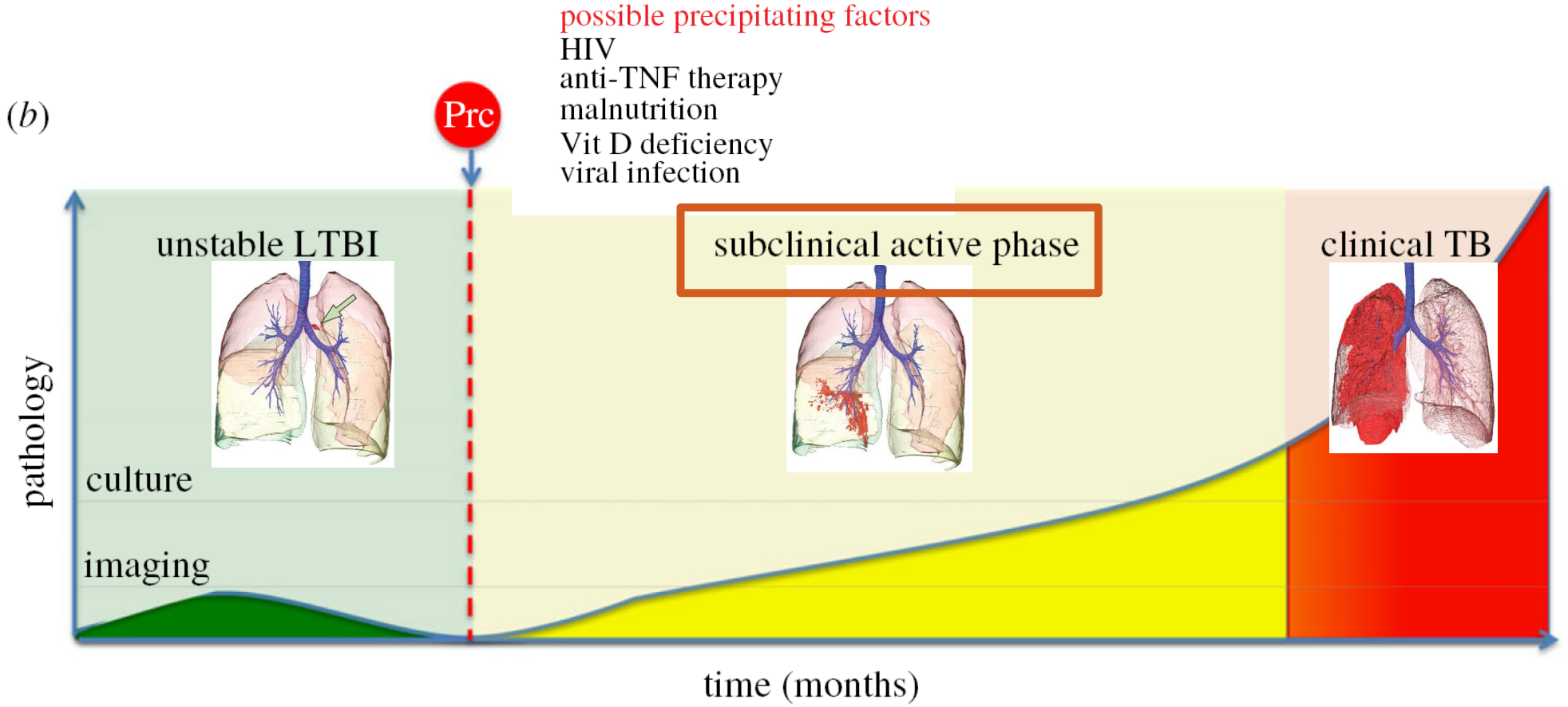


Infection control: Congregate setting and Households

Scopes of infection controls	Contents
Congregate settings	
Managerial activities	Coordinating system for planning and interventions Overcrowding should be avoided Education and communication material for a specific focus
Administrative controls	All inhabitants of long-term facilities should be screened for TB before entry into the facility Referral system for proper management in TB patients in short-term stay such as jails and shelters
Environmental controls	Regulations for ventilation in public buildings Ultraviolet germicidal irradiation (UVGI) could be considered
Personal protective equipment	Same As health-care facilities, Appropriate referral organization in short term stay settings
Households	
Managerial activities	Basic infection control behavior-change campaigns (minimize stigma and the exposure of non-infected individuals)
Administrative controls	Early case detection is the most important
Environmental controls	Natural ventilation may be sufficient
Personal protective equipment	Health care providers should wear particulate respirators when attending MDR-TB patients in enclosed spaces



LTBI Treatment

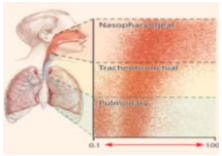


NTT (Numbers needed to treat): the number of contacts to be treated to save one contact from progression to TB disease,

H. Esmail et. al. Philos Trans R Soc Lond B Biol Sci. 2014;369:20130

LTBI Treatment

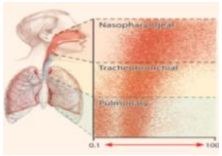
Number needed to treat (NTT)



Kim HJ et. al. IJTLD 2015 19(5):576-581

Table 2 Adjusted HRs for active TB using TST and QFT tests in Cox proportional hazard analysis

	n	Follow-up py	TB cases *n*	Incidence rate /1000 py	HR (95%CI)*	*P* value
After exclusion of cases treated for LTBI						
TST ⩾10 mm			21/5=4			
TST+/QFT+	21	75	5	66.2	35.59 (14.03–90.31)	<0.001
TST+/ QFT−	689	2742	11	4.0	2.05 (1.05–4.01)	0.035
TST+ only	444	1684	17	10.1	5.16 (2.91–9.17)	<0.001
TST−	5714	22360	44	2.0	1	
TST ⩾10 mm			1154/33=35			
TST+	1154	4504	33	7.3	3.85 (2.43–6.10)	<0.001
TST−	5714	22360	44	2.0	1	
TST ⩾10 mm						
TST+/QFT+	21	75	5	66.2	16.82 (5.84–48.46)	<0.001
TST+/QFT−	689	2742	11	4.0	1	



결론

- 결핵의 전염: 비말핵(droplet nuclei)
- 감염: 결핵균전파자 상태, 결핵균의 감염력, 접촉자의 면역상태, 환경적 요인, 사회적 요소
- 감염관리: Health-care facilities,congregate setting, household / Managerial activities, administrative control, environmental control, personal protective equipment
- 잠복결핵 치료 대상자의 확대