

# Contact of tuberculosis at health care facilities in Japan

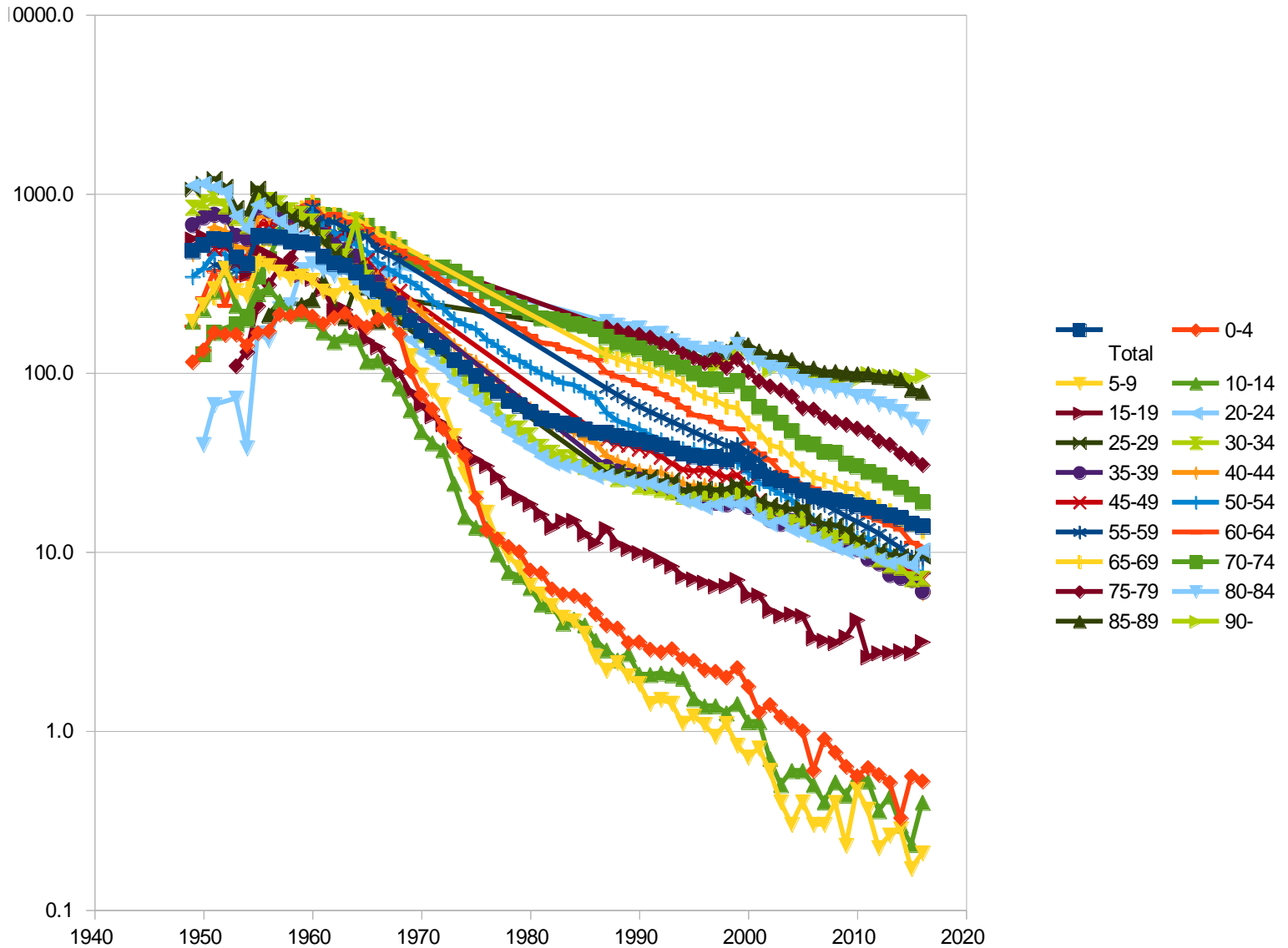
December 8<sup>th</sup>, 2019

Takashi Yoshiyama

Research institute of tuberculosis

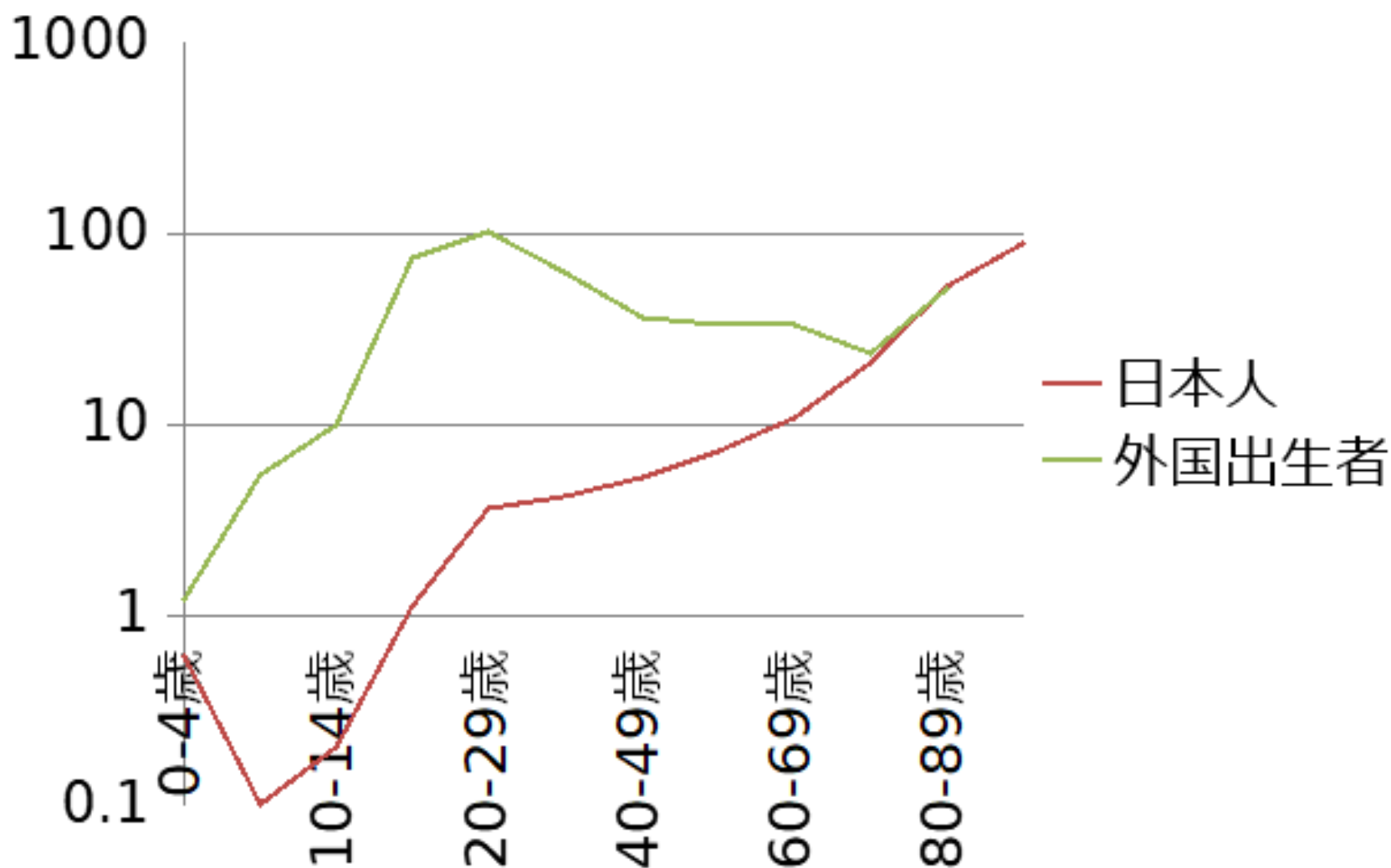
# case detection of TB by surveillance, Japan

## Case detection / 100 000 population, time trend by age



# Case detection of TB by age, Japanese and foreign borne

TB case detection / 100 000, 2017



# Contact of tuberculosis at health care facilities in Japan

1. How important is the hospital acquired infection in Japan?
2. Where does hospital acquired infection occur in Japan?
3. How to control hospital acquired infection.
4. Treatment of latent tuberculosis infection
5. CT scan after IGRA and plain X ray. Is it useful?

# Source of infection with recent transmission in Japan

In Yamagata prefecture, VNTR survey is routinely conducted and 50 clusters with known contact place was investigated.

15 clusters in hospital. (mostly in the ward, one at reception)

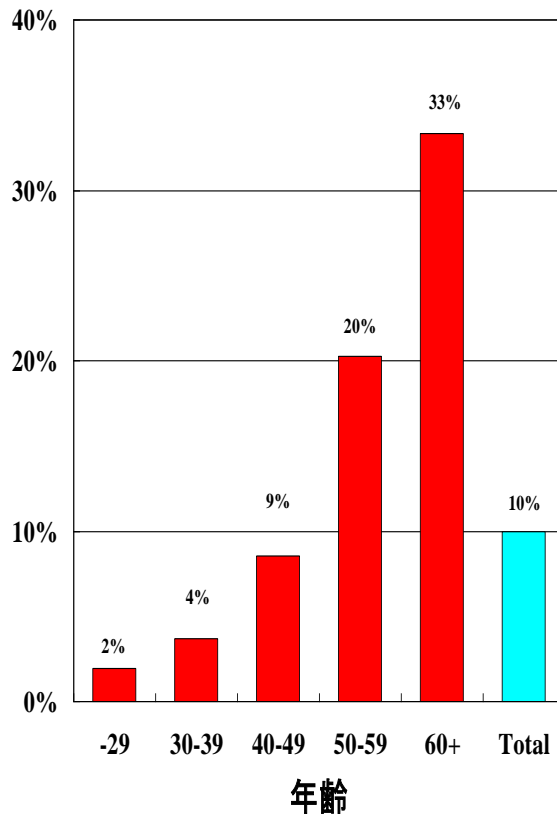
14 clusters at family.

One cluster at nursing home of the elderly.

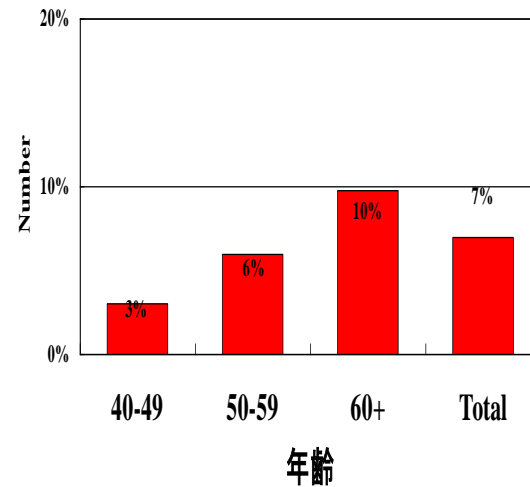
Others are workplace and amusement (Pachinko) shop

Seto J, Wada T, Suzuki Y, Ikeda T, Mizuta K, Yamamoto T, Ahiko T. Mycobacterium tuberculosis Transmission among Elderly Persons, Yamagata Prefecture, Japan, 2009-2015. Emerg Infect Dis. 2017 Mar;23(3):448-455.

## Hospital staff 2003



## General population in Gumma 2003



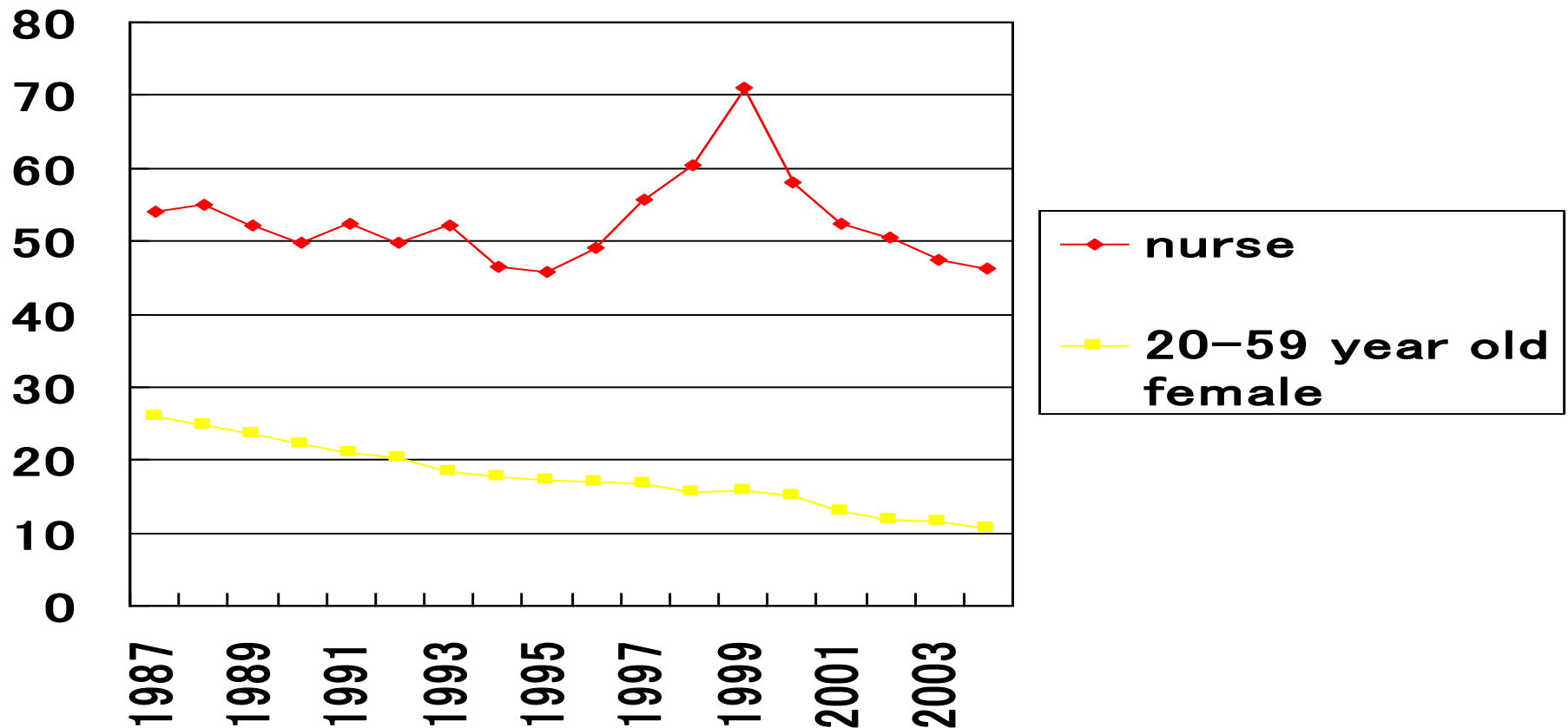
## Age specific IGRA positivity, QFT-G, 2003

Harada et al  
Mori et al;

# TB case in Japan, by age (Japanese in 2018)

age	total Japanese case	HCW	proportion
20-24	70	25	36%
25-29	207	26	13%
30-39	541	23	4%
40-49	883	55	6%
50-59	1059	28	3%

# Incidence rate of TB among nurses



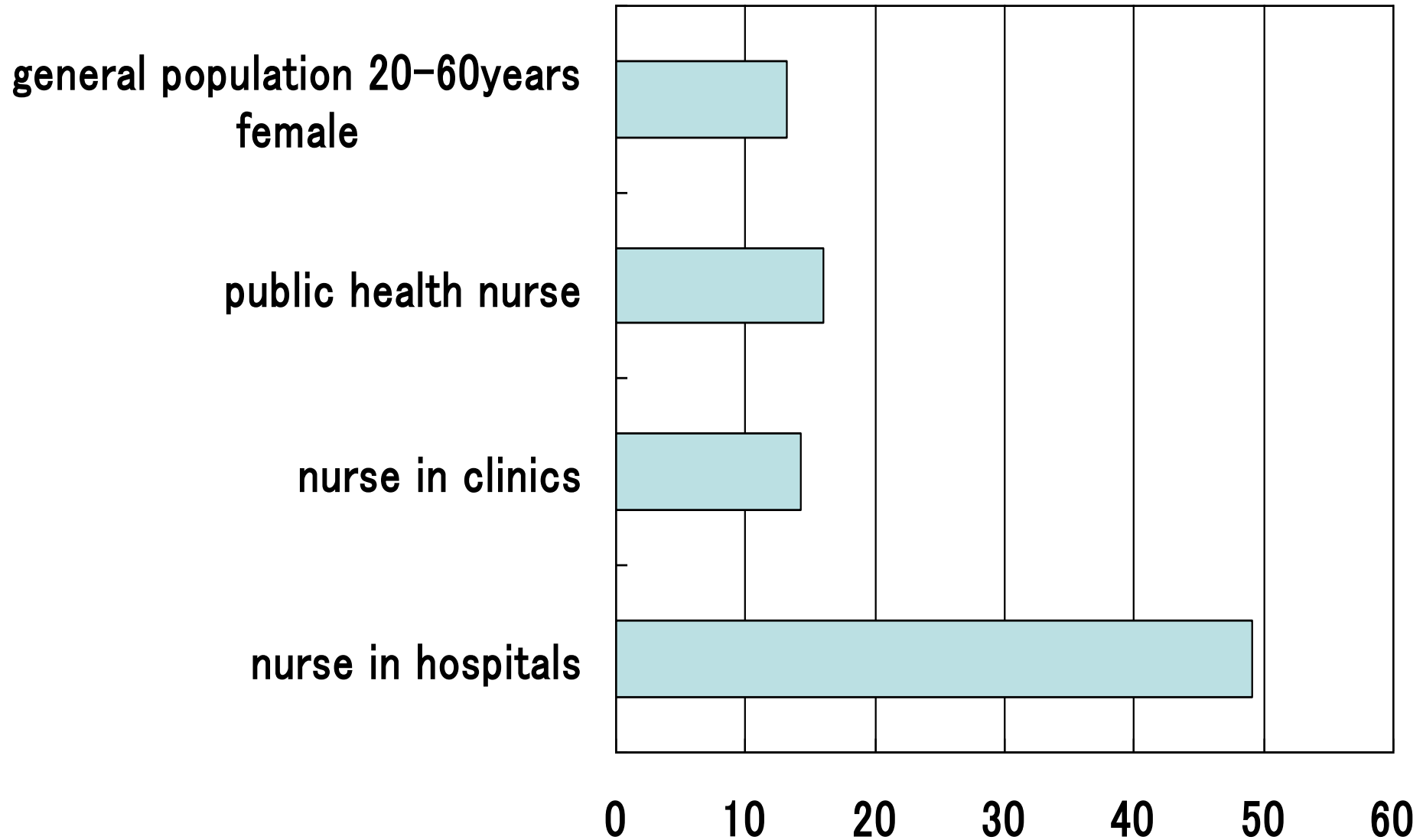
Ohmori, Kekkaku; 2007;85-93



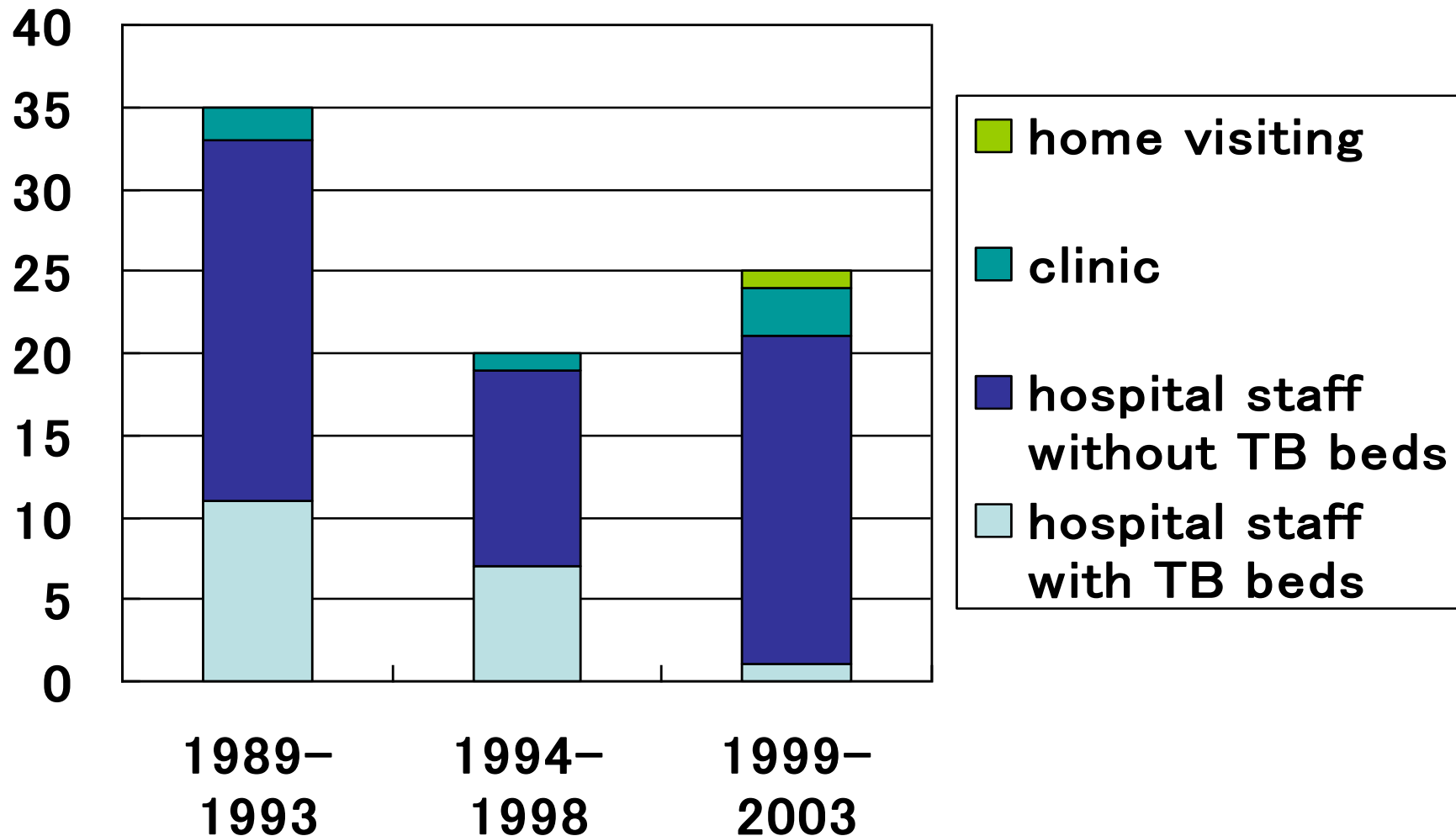
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# Incidence rate of TB among nurses in Aichi



# Incidence of TB among nurses in Aichi



# A source case of HCW infection

Kekkaku 2012;87:635-641

77 year old female, suffering from Rheumatoid arthritis

Jan X, cough and visited other hospital and diagnosed as interstitial pneumonitis.

Admission on 10<sup>th</sup> Jan. In 11<sup>th</sup>, Fiberbronchoscopy findings without TB (smear, NAA of BAL).

Deterioration on 12<sup>th</sup> and steroid pulse therapy.

Deterioration on 31<sup>st</sup> and intubation. Sputum in the trachea was smear 3+ and diagnosed as TB. X ray findings not suggestive of TB on 31<sup>st</sup>.

# Hospital acquired infection

61 contacts that were negative with IGRA in Early Feb were followed up.

19 persons turned to positive with IGRA. (11 after 2 months, 7 after 6 months and 1 after 9 month)

5 case were detected.

One case in early April after IGRA positivity.

One developed TB among those that were not the target of IGRA test due to short contact.

One developed TB among IGRA negative.

One developed TB with INH refusal due to pregnancy.

One staff developed TB among those that resigned that hospital without follow up.

# Other Miliary TB with interstitial pneumonitis

Jan 2016: normal X ray

March 2019: dyspnea on exertion

diagnosis; interstitial pneumonitis. Steroid therapy

August 2019: again dyspnea on exertion

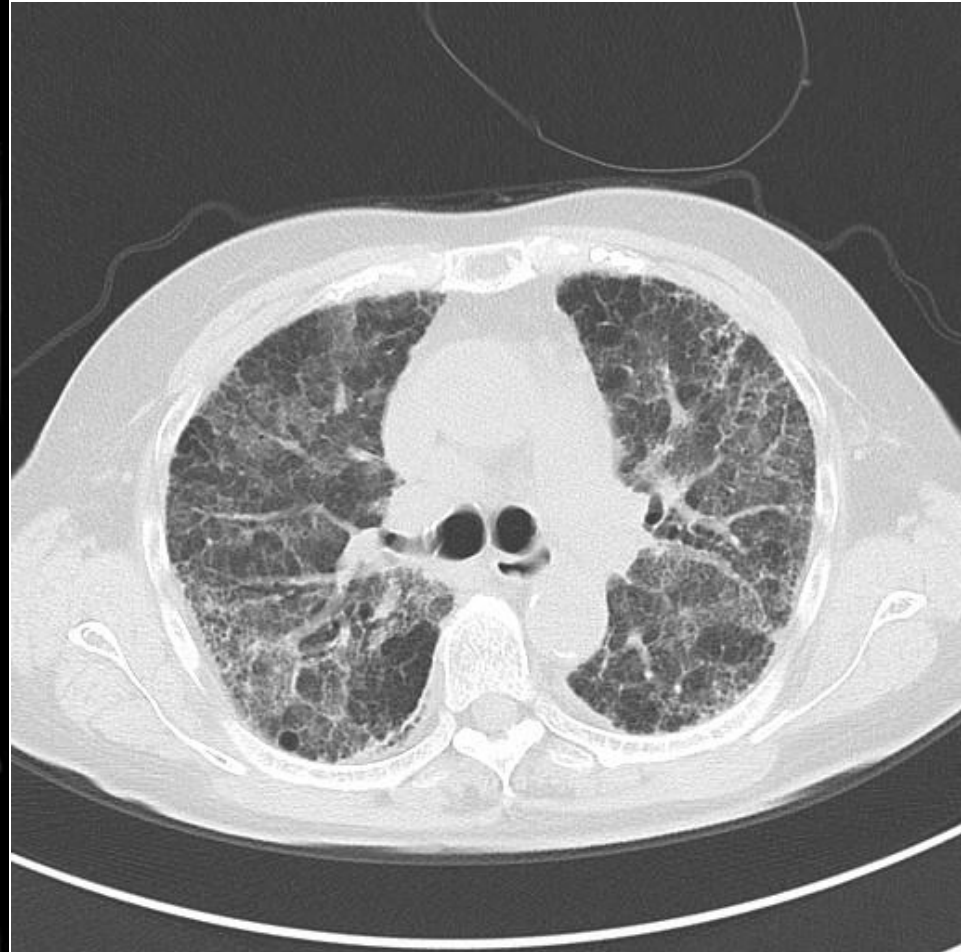
August 26<sup>th</sup>; steroid therapy as deterioration of IP

August 27<sup>th</sup>; T spot TB test N0 A30 B6 M834

September 2<sup>nd</sup> : respiratory failure

September 3<sup>rd</sup>: smear 3+ LAMP TB

March 2019



August 2019, before deterioration





# deterioration



22<sup>nd</sup> August

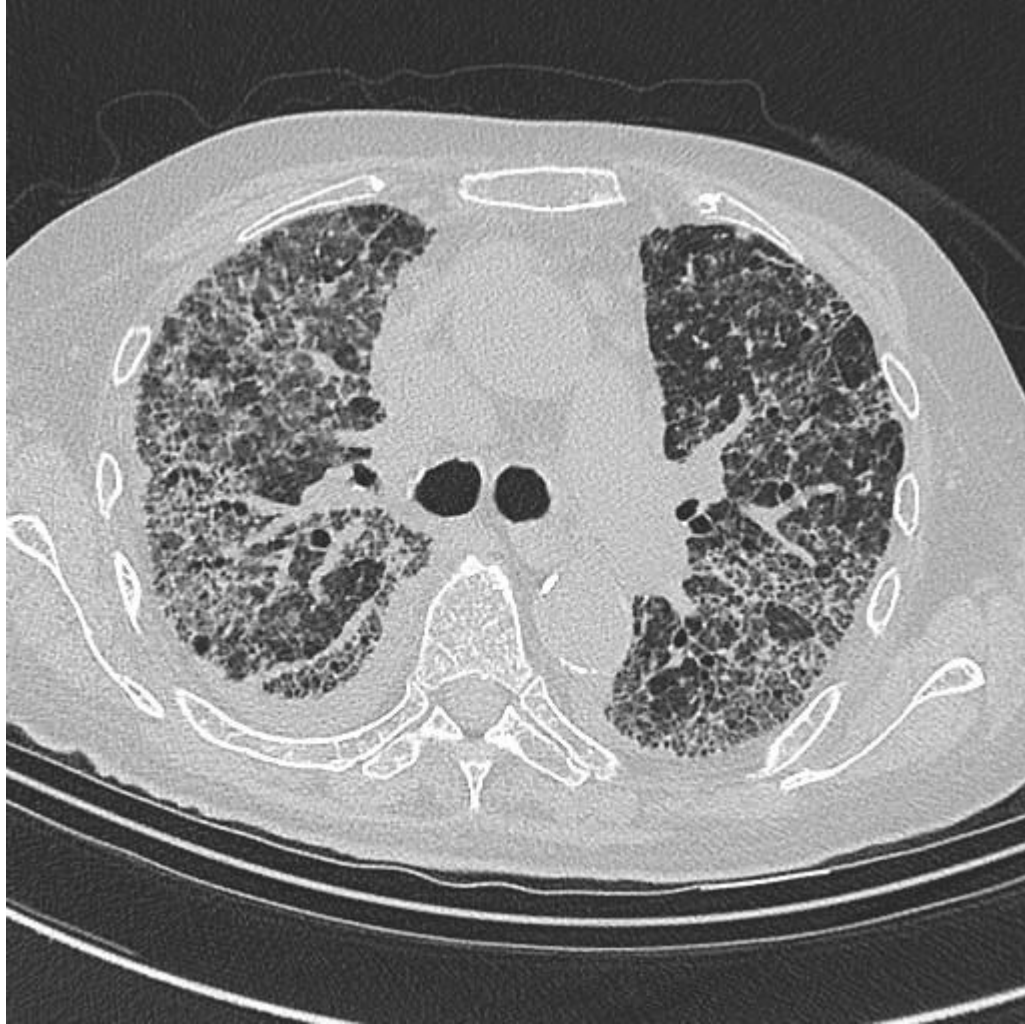


26th  
August



2<sup>nd</sup> September

August 26<sup>th</sup> CT



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# Hospital acquired infection control of TB

1. Policy document, surveillance, training  
(mandatory by medical service law 医療法)
2. early case detection  
(among patients)  
(staff regular health check using X ray)
3. Isolation of bacilli after case detection  
(isolation of cases, engineering, N95 respirators)
4. contact investigation using IGRA  
(contact investigation, regular staff IGRA)

# Hospital acquired infection occurs before diagnosis therefore,

What can we do BEFORE diagnosis?

We need to be careful about procedures that may create droplet nuclei of TB.

- fiberbronchoscopy, sputum suction, etc

Fiberbrochoscopy is done with N95 respirators for all.

This can protect the health care workers but how about patient who will be examined after TB case?

- suspected TB should be done at the last of the day with early smear/NAAT and irradiation with UV

staff regular health check using X ray

x ray examination is mandatory by labor safety hygiene law (労働安全衛生法) for health care workers, teachers, staff of nursing homes, every year.

However, the case detection among HCWs is  $<0.05\%$

Why does it continues?

# Regular health check using x ray is...

Useful but not cost effective

In Fukujuji hospital (500 employee), we have 7 TB cases during the past 30 years.

5 cases detected at regular health check; all sm neg

1 case ; new employee without health check at employment. Symptomatic visit and detected as sm+ cavitory TB.

1 case ; Abnormality detected at regular health check in Jan 2015 (pleural effusion) and July 2015 (adhesion) but no further investigation because he did not go for investigation. Detected as military TB in August 2015 with symptomatic visit. Sm +

# Contact investigation at hospital acquired infection

Target

No definite criteria.

Usually, stone in the pond = first, contact of TB cases in the same room. If many IGRA positive or any new TB case, expand the contact investigation.



# Contact investigation at hospital acquired infection

In F hospital, from 2005 to 2019,  
among 18 TB cases detected after admission at pul.  
ward,  
289 contacts were identified.

Among 70 contacts in the same bedroom (patients),  
no contact converted from negative to positive.

Among 219 staff with contact, two contacts turned  
to positive.

(turned from negative soon after detection but  
turned to positive 3 months later)

# bacillary TB cases isolation

sputum smear positive TB cases-isolation is mandatory by law. Mostly at the specific isolation rooms for tuberculosis or rooms for infectious diseases . (infectious diseases control law)

sputum smear negative TB cases are usually treated ambulatory. However, if the case is in serious condition, the case is hospitalized and NAA positive (or culture positive) TB cases are hospitalized in rooms for tuberculosis, infectious diseases or general.

# Infectiousness of chronic cases

## TB cases among household members (1980s in Japan)

Susceptible?	Hp or OPD?	observed	Contact PYs	breakdown
Susceptable	hospitalized	127	823	10(1.22/100PYs)
Susceptable	OPD	32	270	2 (0.74/100PYs)
Chronic	hospitalize	129	1138	6 (0.53/100PYs)
Chronic	OPD	58	377	5(1.33/100PYs)

# airborn infection isolation rooms

Number of sputum  
smear positive TB cases  
in decreasing in Japan

2013;7584

2014;7153

2015;6676

2016;6281

2017;6031

2018;5485

Number of airborne  
isolation rooms by survey in  
2018

(participation rate was  
around 50%)

total; 1822

room for TB: 1395

(total room for TB 1827)

room for infe. dis.: 421

kekaku; 2019:in press

Air isolation room





anteroom

待合室

押

## Sputum induction room in the Air isolation room area





## Elevators for TB cases

4階専用

51~466

A病棟

01~325

B病棟

01~217

相談室 在宅医療室

診療 薬局 事務部

診療科 臨床検査科

放射線科 歯科

時間 全日 11時~20時

面会の方は  
受付をおたずね下さい。

4階の患者様は  
4階専用エレベーター  
(売店前)をご利用下さい。

事務部長



Air exchange with HEPA filtration in the elevetor



Air exchange with HEPA filtration in the elevetor





## Entrance of TB isolation area, N95 for visitors



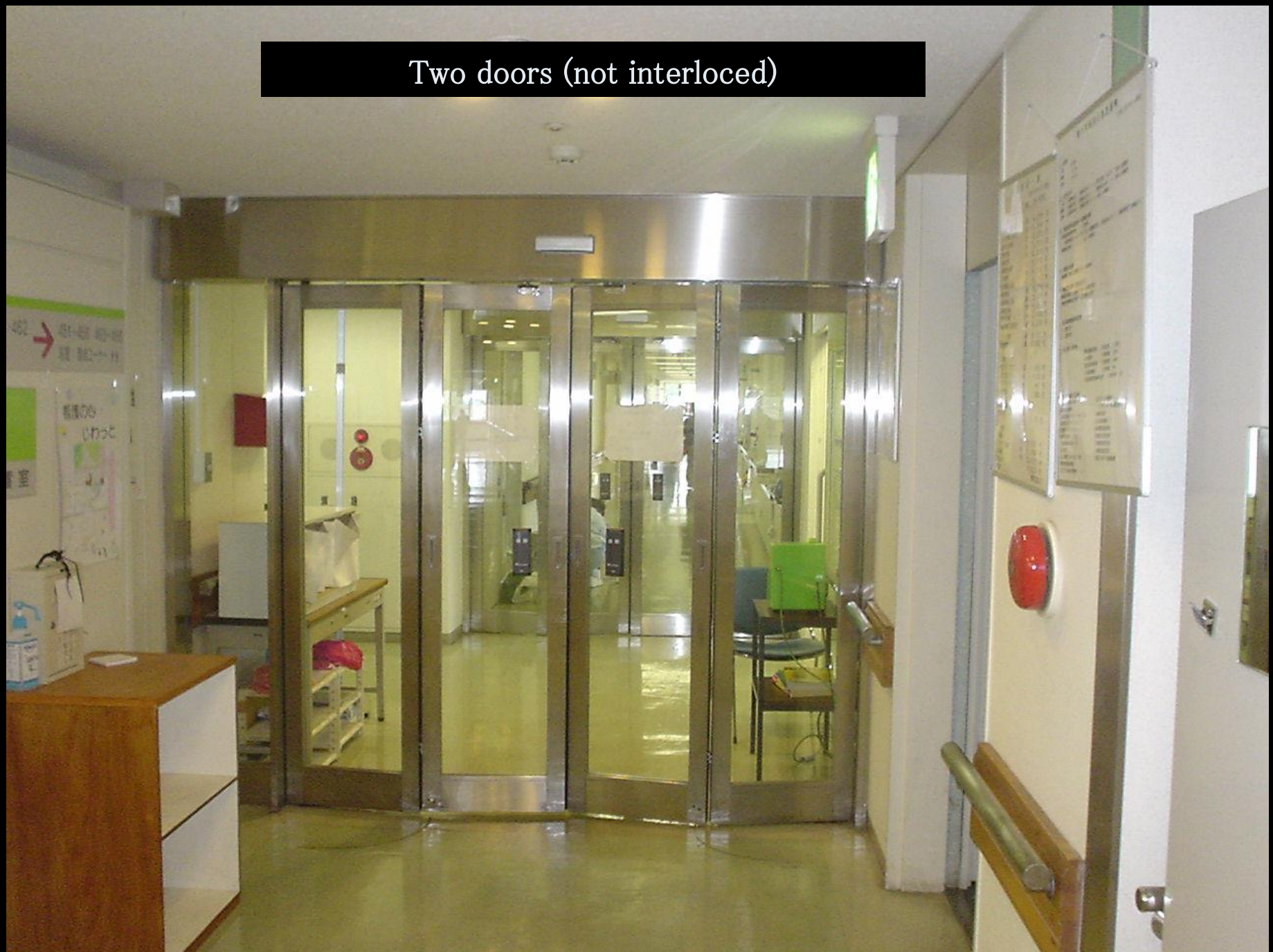


N95 for staff





Two doors (not interlocked)



HEPA filter air cleaner in TB ward





N95



# Fit test



To be done if you change the shape / you try new respirator



# Roken siki Mask fitting tester



Count the particles  
within and  
outside of the  
respirator

850 000 Yen

# Reinfection

Re infection is reported in Moldova

(Int J Tuberc Lung Dis 2015;19:1520-23)

Among pan susceptible TB admitted to TB hospitals, 5.1% cases developed MDR TB later.

Among these 75% of MDR strain were identified with genetically distinct from the original pansusceptible stain.

# Re infection in Fukujuji hospital

Cases that were infected in TB ward (1985-2015)

contact	admission	py	MDR infection (prop)	
MDR-TB	676	299	0	0
non MDR-TB	8342	1661	0	0
NTM	2728	334	2	0.1%

(0–1.36/100 person years)

(There were three cases that developed MDR TB after admission as non TB diseases (NTM). Among these, one case was with unknown source)

# Hospital acquired infection of MDR TB

Kobayashi et al Kekkaku 2013;88:477-484

Source case, before TB

1987 diabetes mellitus

1999 pan susceptible tuberculosis, treated with INH, RFP and EB and cured with 1 year treatment.

2002 renal failure and hemodialysis。

# Hospital acquired infection of MDR TB

Kobayashi et al Kekkaku 2013;88:477-484

## Source case

May 2006, with the diagnosis of pneumonia, treatment with LVFX for 2 weeks

June 2006, diagnosis with TB. INH, RFP and SM. Was known to be RFP and SM resistance in August

August 2006. INH, EB, PZA, KM

September 2006 INH, EB, PZA (ear problem)

February 2007 smear positive but X ray no change

June 2007 known to be MDR TB and started treatment with Cs, Pas, PZA, SPFX, EVM and cured

# Hospital acquired infection of MDR TB

Staff A : Nov 2007, QFT+, Dec 2008 XDR TB

Staff B: Nov 2007 QFT-, Feb 2009 QFT+, April 2010 XDR TB

Staff C: Nov 2007 QFT-, Feb 2009 QFT $\pm$ , July 2010 QFT+, Jan 2011 XDR TB

Staff D: Feb 2009 QFT-, Dec 2010 X ray normal, May 2011 QFT pos and XDR TB

Staff E: Nov 2007 QFT-, Dec 2010 X ray normal, June 2011 QFT pos and July 2011 XDR TB

Family of A: Feb 2009 QFT $\pm$ , July 2010 TB diagnosis with culture negative

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## 4. Treatment of latent tuberculosis infection

Basically done with 6 months isoniazid until now.

(Rifampin is only for cases with isoniazid adverse reaction or resistant source and Rifapentin is not available in Japan).

Japan TB society recommended (Nov 2019)

Isoniazid for 6 months

Isoniazid + Rifampin for 3 months

Rifampin for 4 months

Rifapentin is not used in Japan.

For contact of drug resistant TB :no standard (LVFX)



# Adverse drug reaction of isoniazid treatment

	isoniazid n	stop Ison with liver dysfunctio n	AST/ ALT>500	p value	AST/ ALT>1000 and T bil>3	p value	due to liver dysfunctio n	p value
total	1494	185 12%	47 3.1%		9 0.6%		14 0.9%	
male	700	78 11%	18 2.6%	ref.	1 0.1%	ref.	4 0.6%	ref.
female	794	107 13%	29 3.7%	0.30	8 1.0%	0.03	10 1.3%	0.08
age distribution								
<15	94	1 1%	0 0.0%	ref. (0-29 years old)	0 0.0%	ref. (0-29 years old)	0 0.0%	ref. (0-29 years old)
15-19	29	1 3%	0 0.0%		0 0.0%		0 0.0%	
20-29	158	4 3%	0 0.0%		0 0.0%		0 0.0%	
30-39	213	17 8%	2 0.9%	0.19	1 0.5%	0.43	2 0.9%	0.19
40-49	203	39 19%	8 3.9%	0.001	1 0.5%	0.42	2 1.0%	0.18
50-59	231	48 21%	15 6.5%	0.000	2 0.9%	0.20	4 1.7%	0.04
60-69	307	57 19%	18 5.9%	0.000	5 1.6%	0.04	6 2.0%	0.02
>70	259	18 7%	4 1.5%	0.05	0 0.0%		0 0.0%	
contact	1130	153 14%	40 3.5%	ref.	8 0.7%	ref.	12 1.1%	ref.
immunosuppression	111	8 7%	1 0.9%	0.1	0 0.0%	0.47	0 0.0%	0.32
immunosuppression thera	243	19 8%	5 2.1%	0.33	0 0.0%	0.21	1 0.4%	0.3
contact at household	355	51 14%	15 4.2%	ref.	3 0.8%	ref.	5 1.4%	ref.
contact at workplace	329	47 14%	13 4.0%	0.99	3 0.9%	0.99	2 0.6%	0.51
hospital	139	16 12%	2 1.4%	0.21	0 0.0%	0.37	0 0.0%	0.19

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# TB case after isoniazid (contact)



2009/11/29(before TLTBI), 2012/6/8



2012/12/27 (at clinical TB, s+c+ H resist)

## CT findings at contact investigation

TB case detected by CT (X ray normal) at contact examination

hospital	total contact	no CT	CT	TB detected with CT	
A	31	0	31	11	(35%)
B	46	33	13	1	( 8%)
C	16	1	15	3	(20%)
D	106	46	60	6	(10%)
F	13	1	12	1	( 8%)
H	46	16	30	2	(7%)
I	38	0	38	3	(8%)

# Is CT meaningful for prevention of bac TB?

at treatment of latent TB

clinical TB during follow

with diseases

no diseases

no CT scan	0	519	6
with CT scan	27	1024	4
(among contact)			
no CT scan	0	468	6
with CT scan	27	700	1 (significantly reduced)

kekkaku 2018;93:447-457

# Is CT meaningful for prevention of bac TB?

	total	TB findings at beginning	no TB findings at beginning	clinical TB during follow up
without CT	243	0	243	5
with CT	229	24	205	3

CT: computed tomography, TB; tuberculosis

Journal of infectious disease chemotherapy d 2019; May 14. pii: S1341-321X(18)30326-X. doi: 10.1016/j.jiac.2019.03.023.

# Fukujuji contacts, CT findings

2005 outbreak (all culture negative)

nodule under pleura : 1

centrilobular micronodule : 5

2008-16

TB cases

bacillary

non bacillary

centrilobular micronodule

4

10

nodule under pleura

1

1

infiltration

1 (parabronchial

1

fibrotic

2

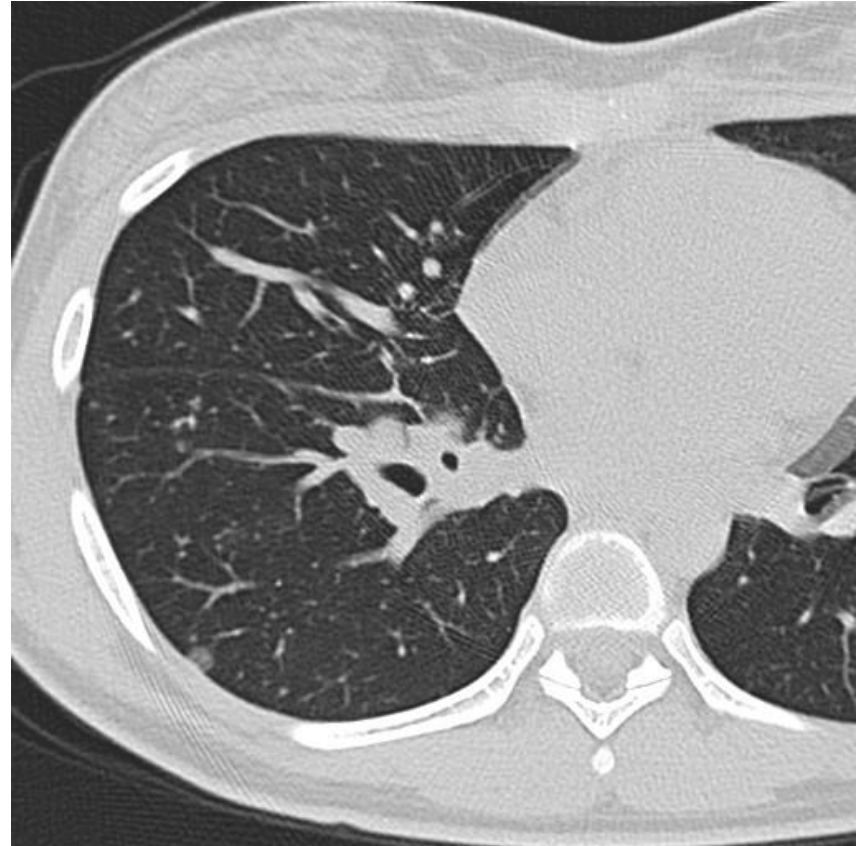
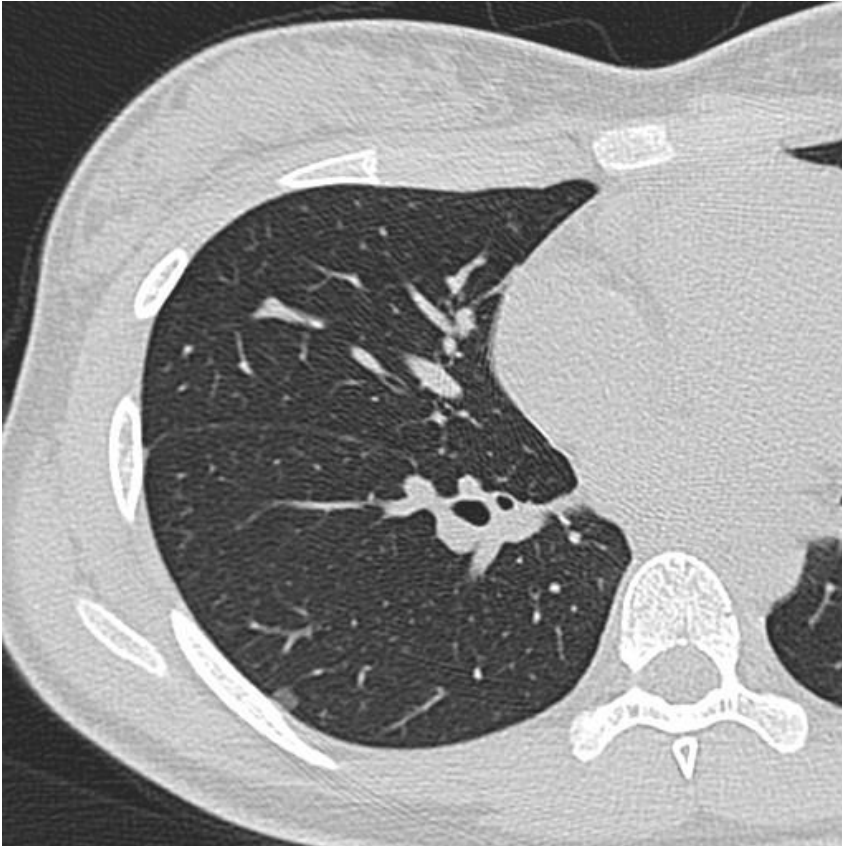
GGO

2

Kekkaku 2008;83:411-416

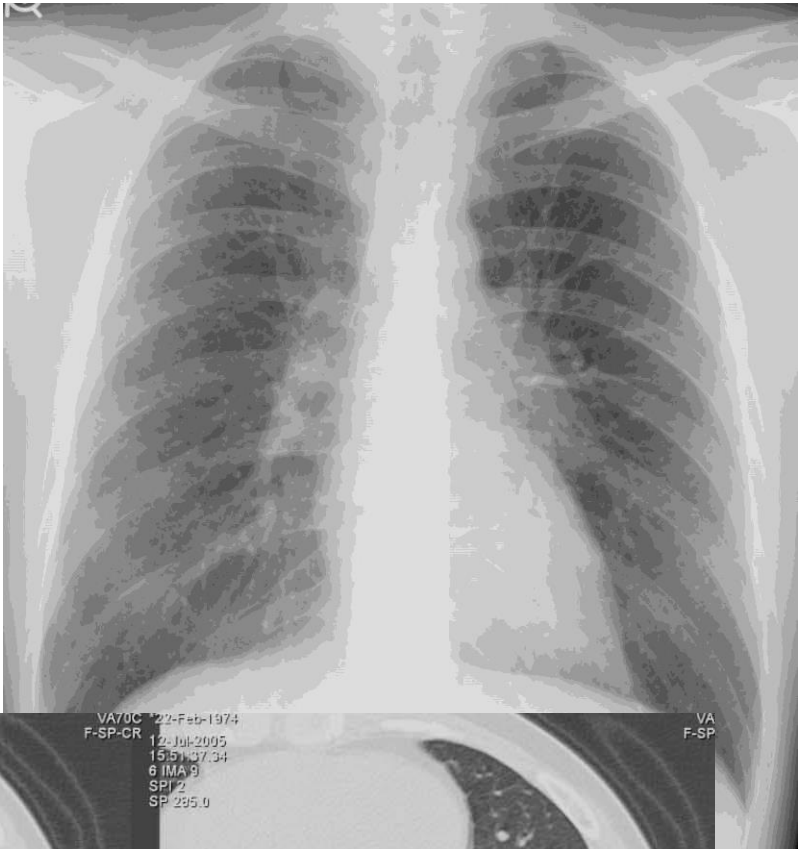
kekaku 2018;93:447-457

Fig 4-1 (Ground grass opacity was detected at contact examination and was treated as latent tuberculosis infection because the ground grass opacity was not considered as active tuberculosis), Fig 4-2 (After completion of treatment of latent tuberculosis infection, the contact developed clinical tuberculosis and the ground grass opacity was not changed)

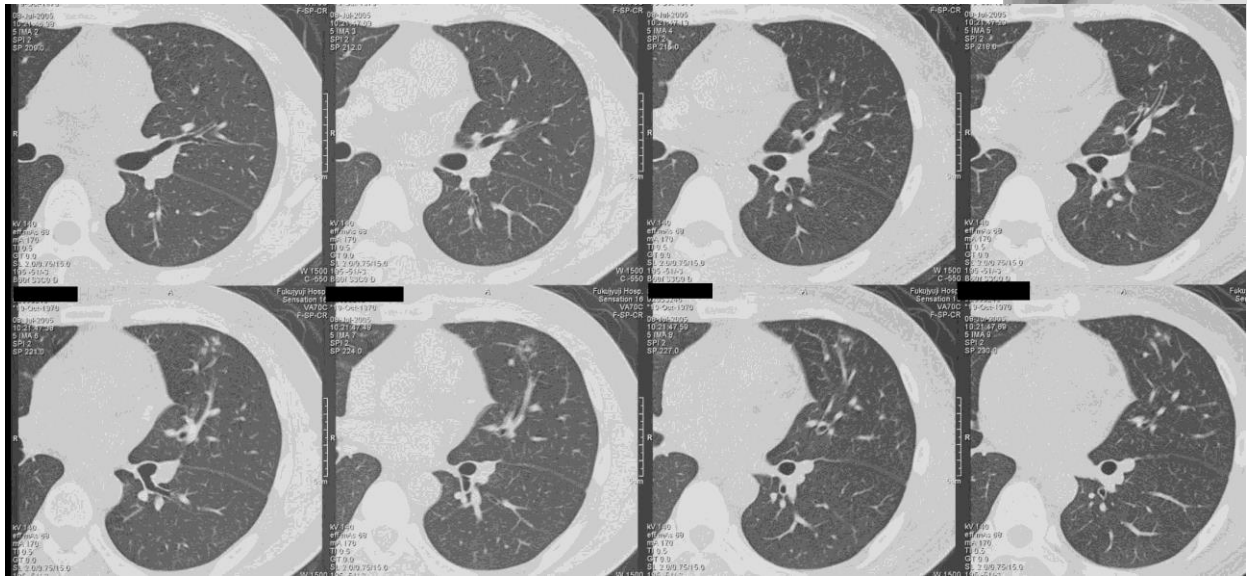




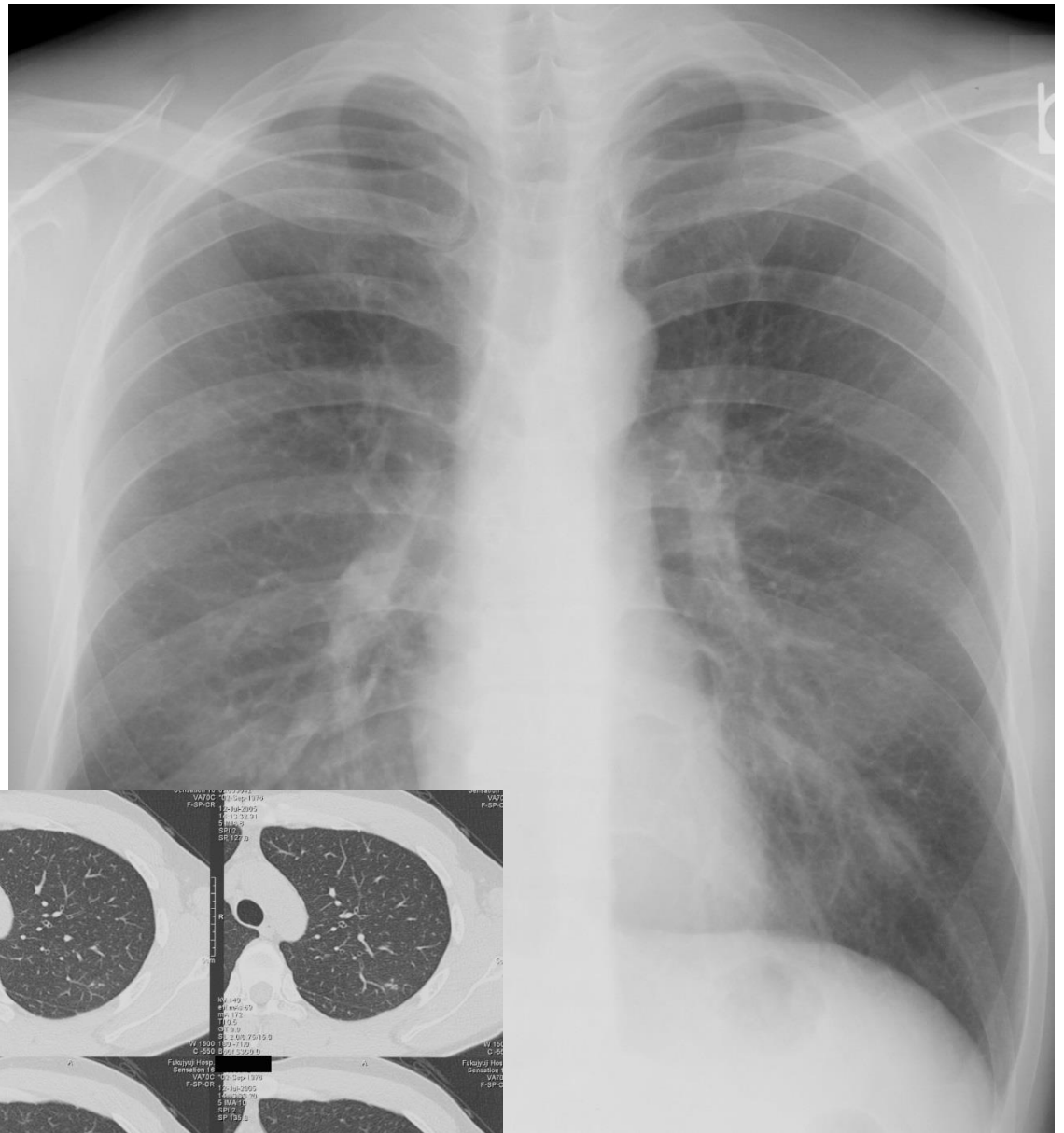
subpleural, culture negative, contact investigation at an outbreak



centrilobular micronodule, culture negative,  
contact investigation at an outbreak

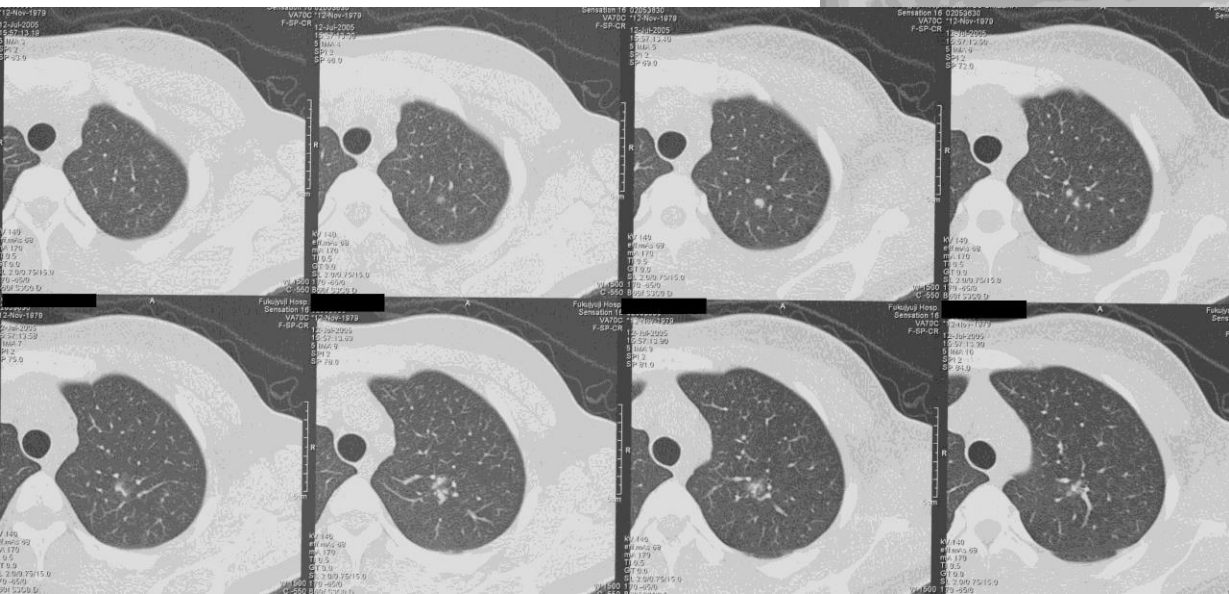


centrilobular micronodule,  
culture negative, contact  
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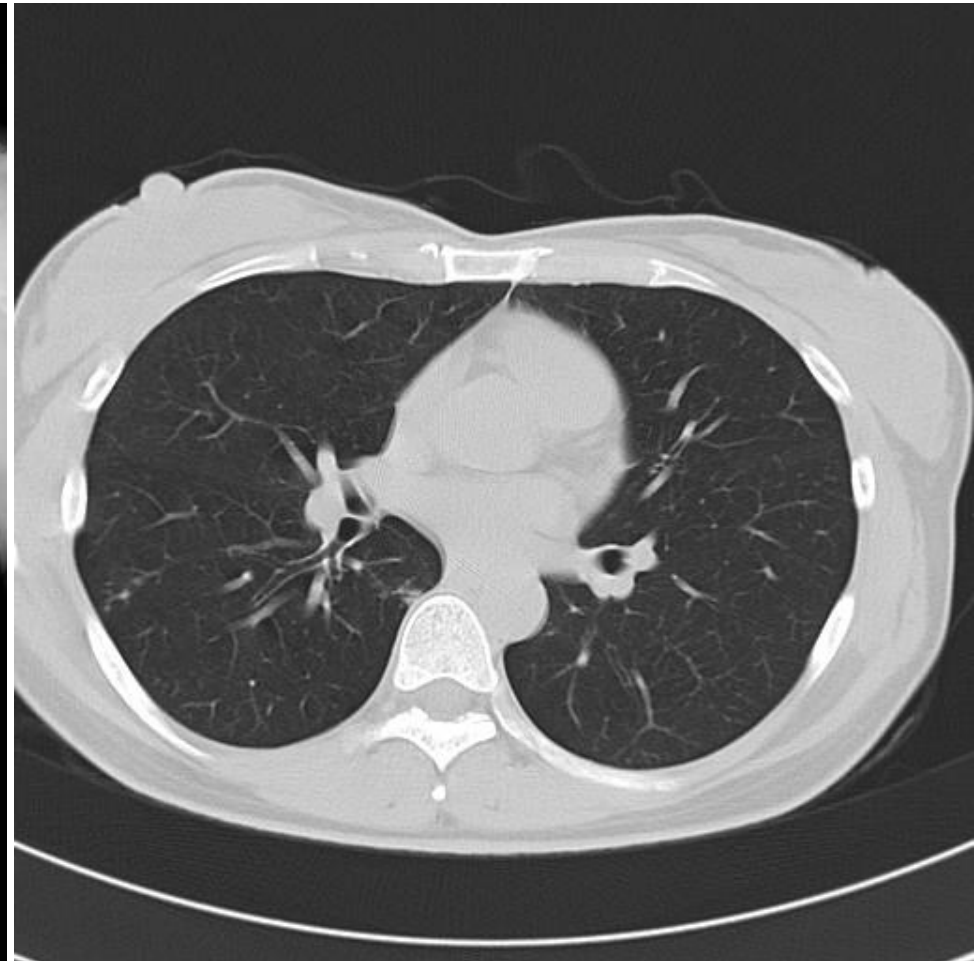




centrilobular micronodule,  
culture negative, contact  
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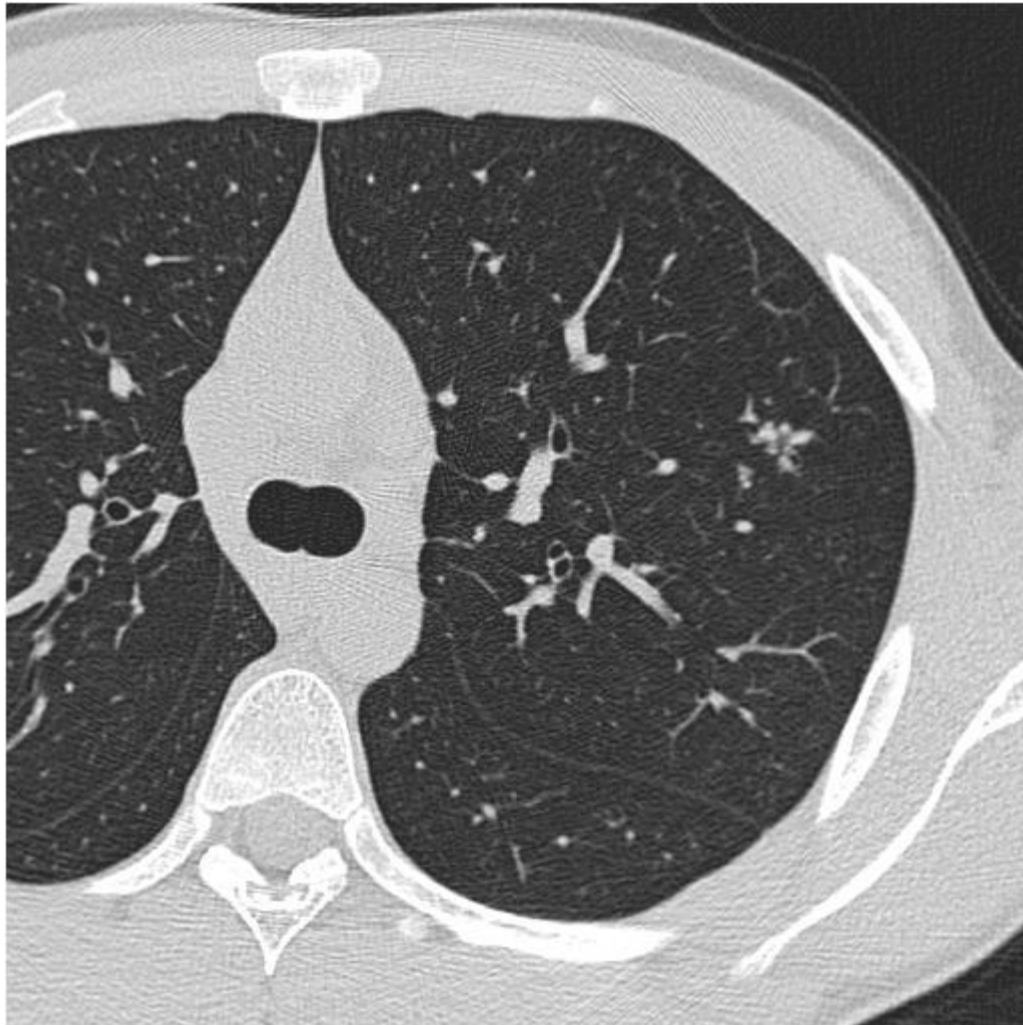


40 year female, wife of TB, contact investigation 3 months after  
detection of TB <husband> was IGRA positive, with fever and sputum



sputum culture (MGIT) was positive at 16 days and changed regimen from H to HRZE

# contact of MDR TB, 15 years old



X ray normal

culture positive with gastric  
aspirate

Resistant to INH, RFP, PZA, EB, SM  
Treatment with KM, LVFX, Cs, PZA  
(index case was susceptible to  
PZA)

# CT findings before bacillary TB

Han et al IJTLD 2019;23:698-706

23 cases of bacillary TB with CT scan 3 month before

nodule	19
centrilobular micronodule	7
bronchiectasis	1