

2nd Global Symposium on IGRAs, May 30 – June 1, 2009, Dubrovnik

IGRAs in HCW

Uses in an Intermediate Burden Setting

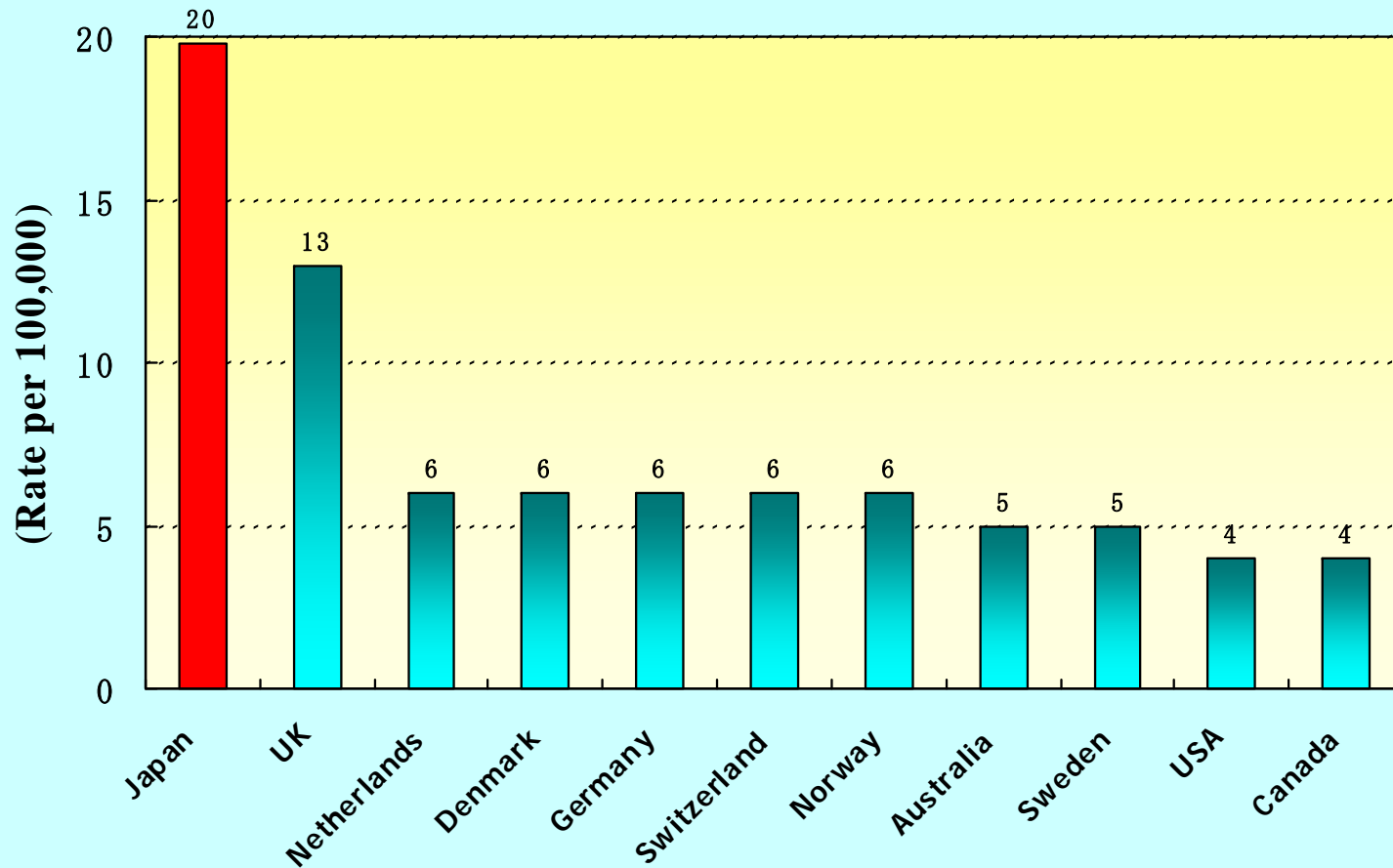


Toru Mori

Research Institute of Tuberculosis
Japan Anti-Tuberculosis Association

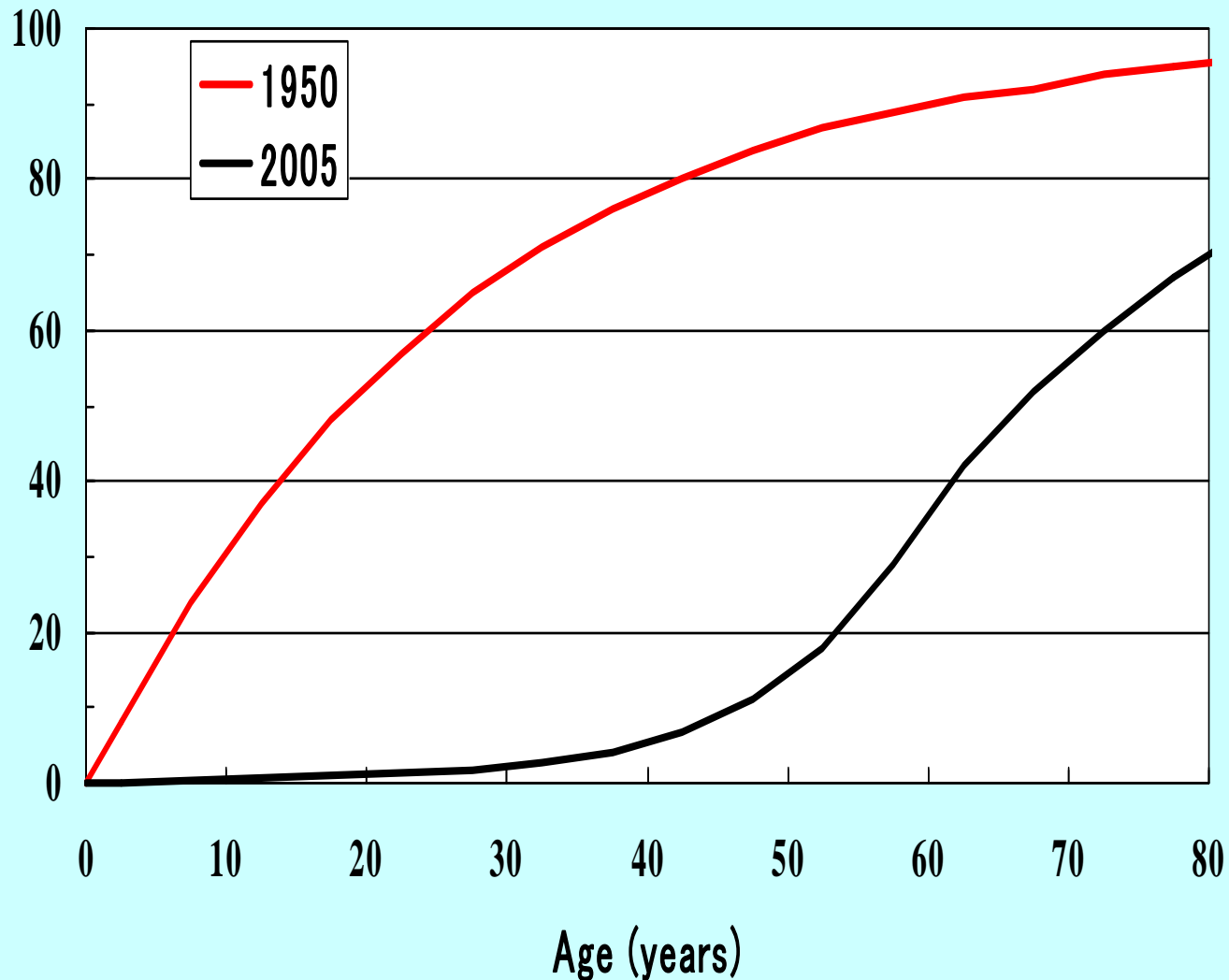
Japan as an "Intermediate Burden Country"

(Notification rate, All forms; 2007)



Age-specific Prevalence of TB Infection

(Estimated, Years 1950 & 2005)



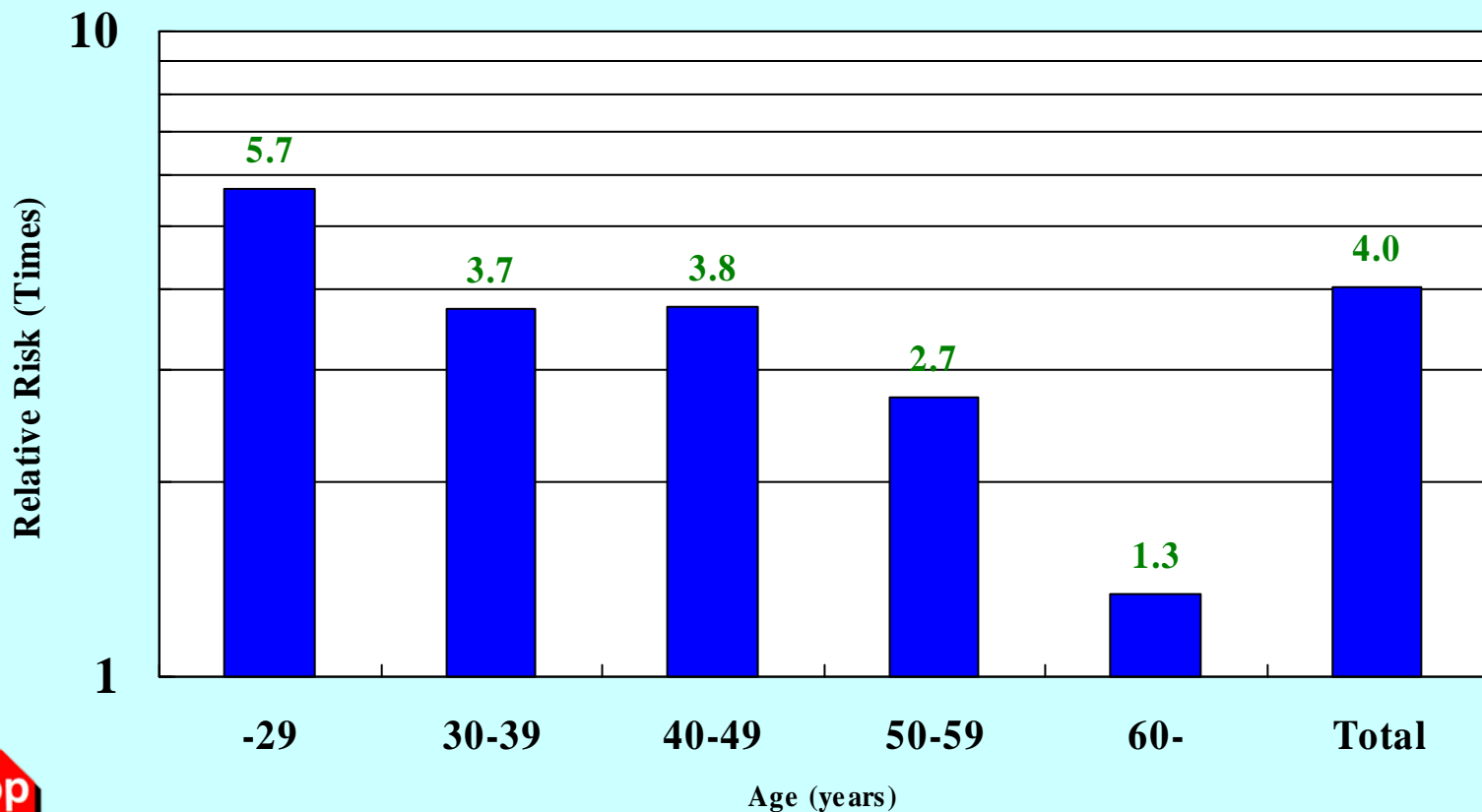
A case of nosocomial TB transmission

- Index case: A doctor, aged 27 yrs, under a training program in a hospital. Early February she attended **bronchoscopy** of a patient with rheumatic arthritis and pulmonary fibrosis under **steroid** therapy. The patient was diagnosed with **smear+ TB**, and died soon.
- Late March a contact investigation was performed to 62 HCWs and 6 patients that revealed **2 active TB and 12 LTBI cases**. The index case was **QFT-negative**.
- In March she moved to another hospital for training in the obstetric department. She developed **cough and fever, lasting 4 weeks** and finally diagnosed as TB with **positive PCR**. A contact examination was performed to ca. 150 contacts including **60 newborns** she had seen. **No new case nor LTBI** was detected.



TB Risk of Female Nurses

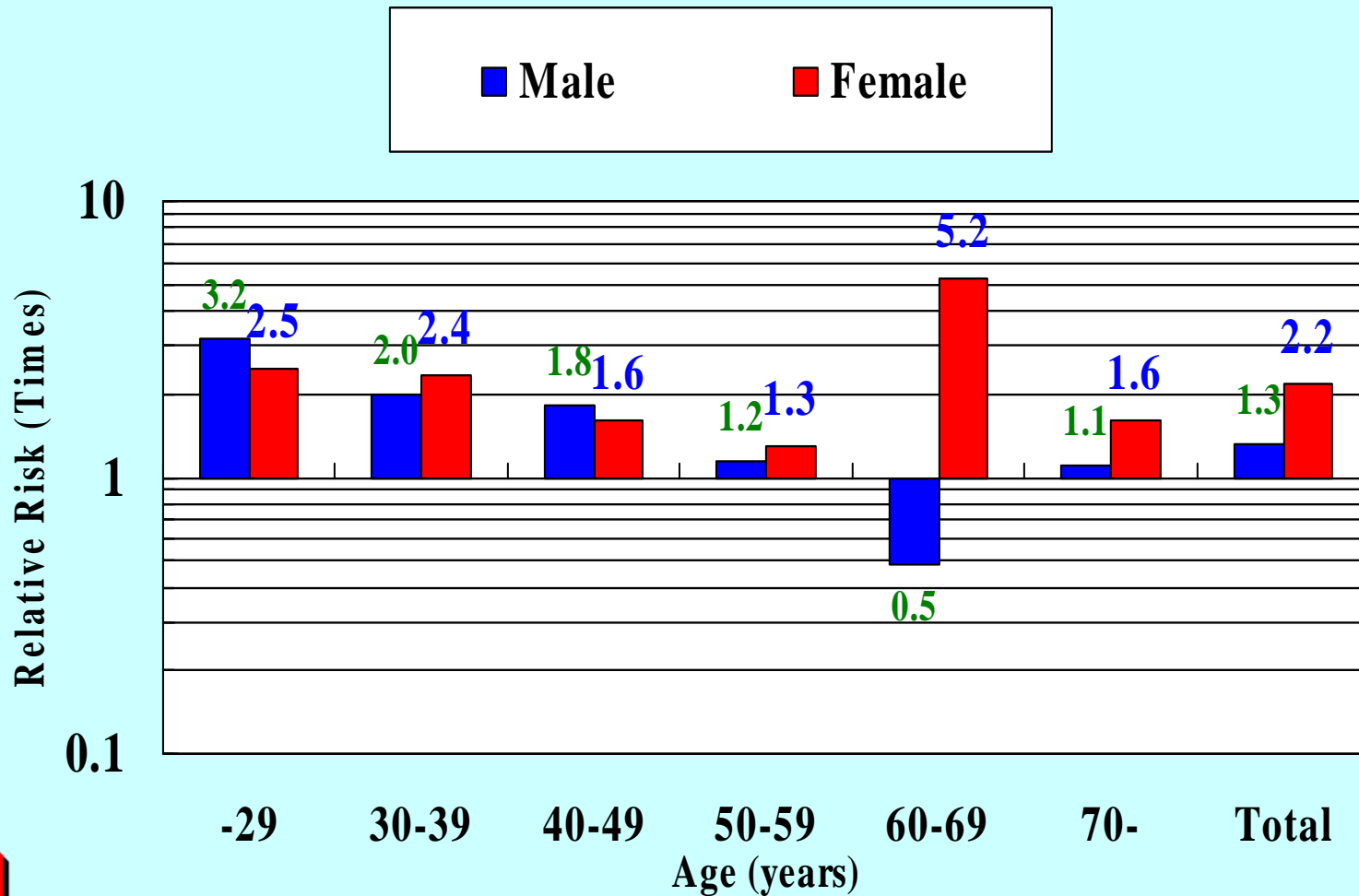
(Japan, 2007)



(TB Surveillance Report, 2007)

TB Risk of Doctors

(Japan, 2007)



(TB Surveillance Report, 2008)

HCWs as a Danger Group

- A Potential Infection Source to **Vulnerable people**
 - Newborns, Young infants
 - Immunocompromized patients
 - Aged subjects
 - HIV-infected, Diabetics, Immunosuppressive therapy
 -

Guidelines for TB Control for HCWs

(Jap. Soc. TB, 1997-)

- On employment
 - Two-step TST, as a baseline
 - BCG (?) if TST is negative
- Periodically
 - Chest X-ray (Annual, mandatory)
- Contact action
 - TST, compare with a baseline
 - Chest X-ray for Positive TST

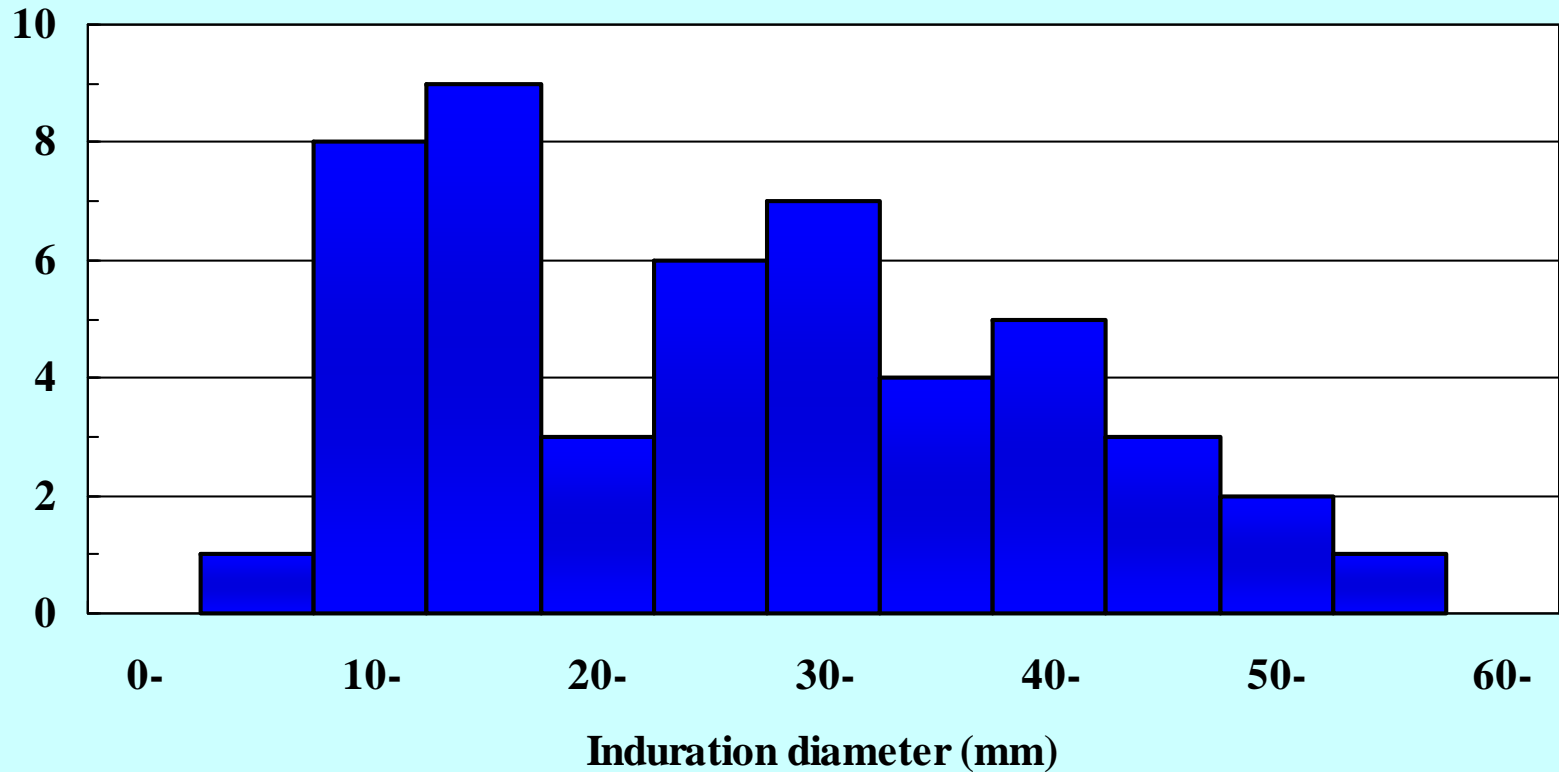


A Case of a Community General Hospital

- A Prefectural Govt Hospital
- Population under service: 54,000
- New TB cases (Community) :12/yr (average)
- Beds: 309 (TB 7, Infection 3)
- Staff: Total 479 - Doctor 39, Nurse 193, Lab/Radiology/Other technical 46, Clerical & Other: 97, Mean age: 40.8 years

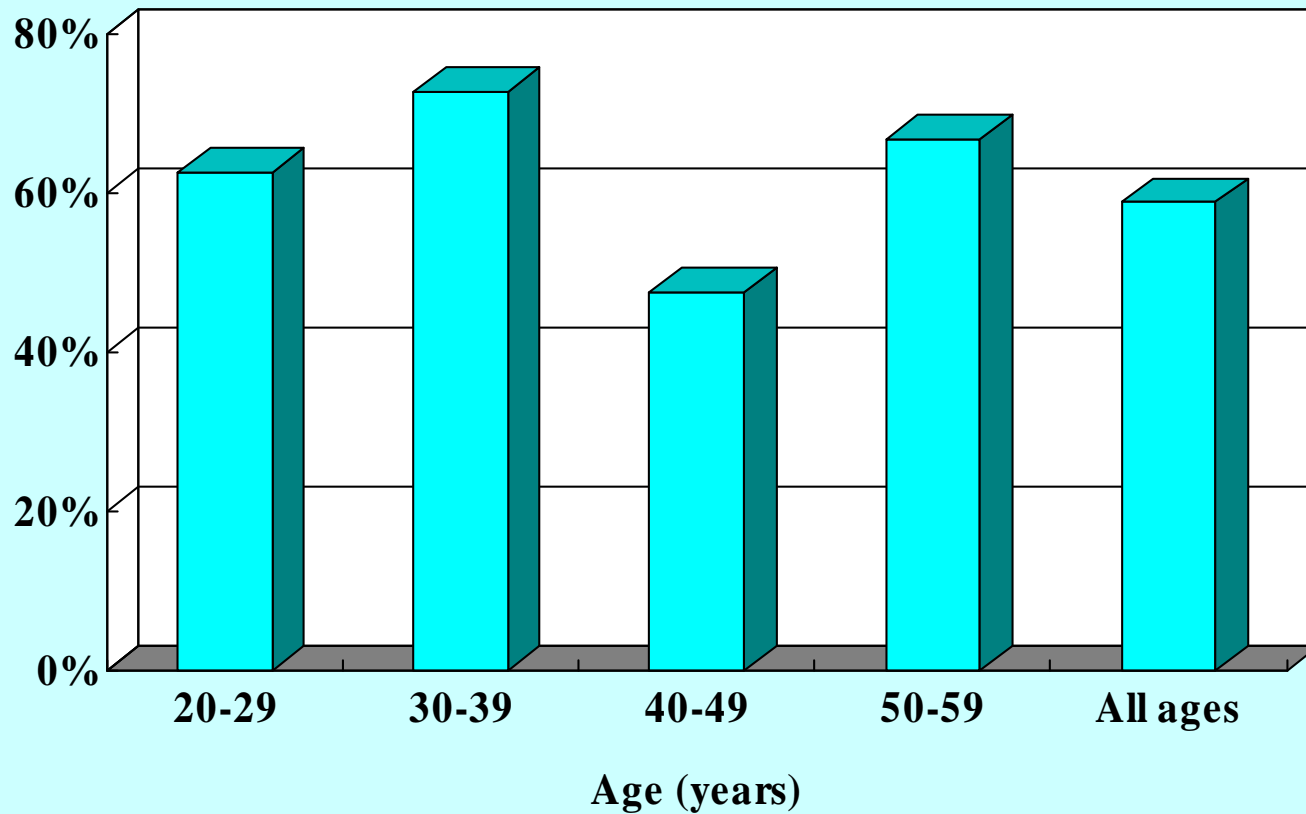


Mx Reaction Distribution of HCWs



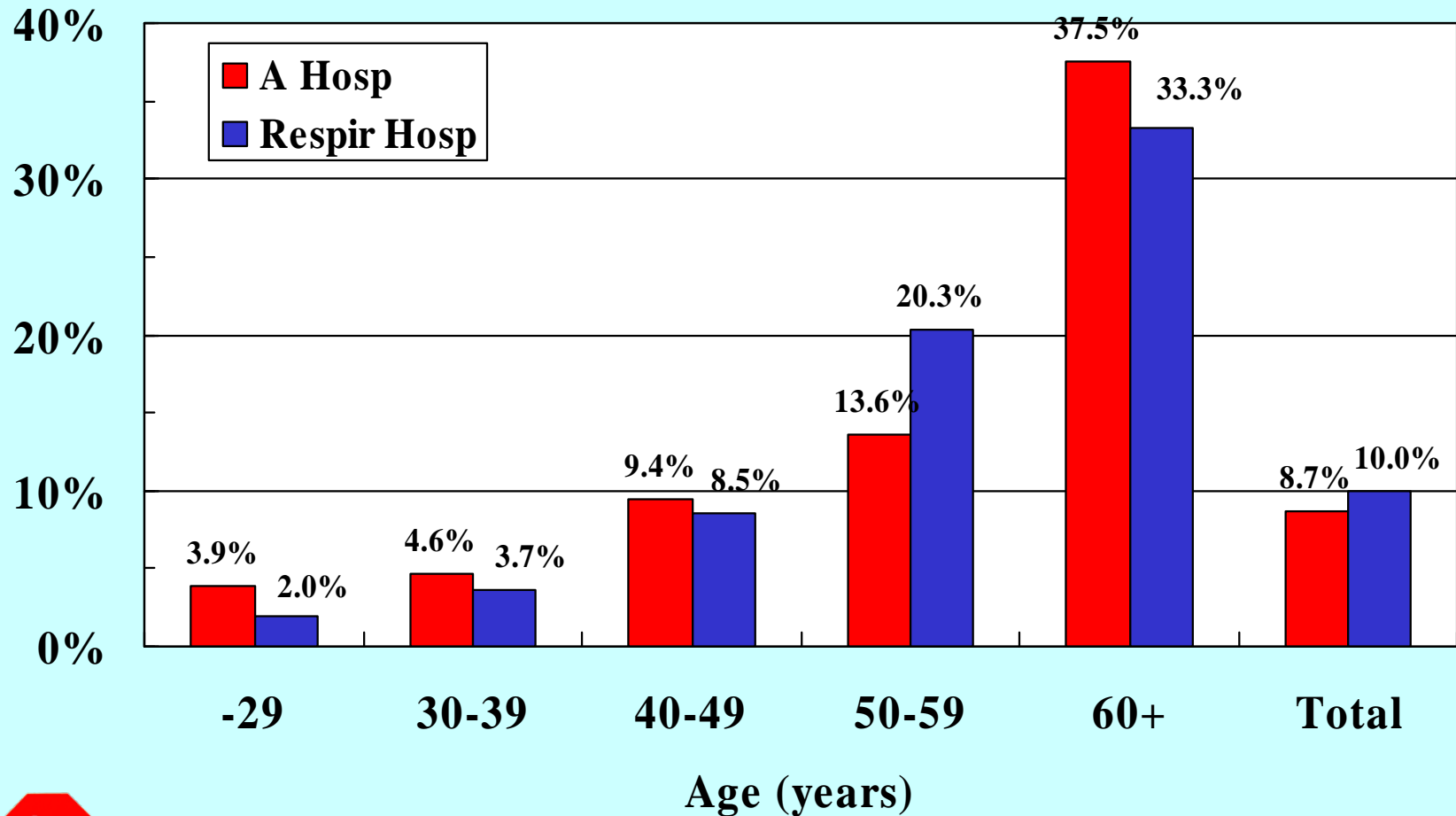
Strong TST is a surrogate of **Infection ?**

(Strong TST: Induration $\geq 20\text{mm}$)



Age-specific QFT-G Positivity

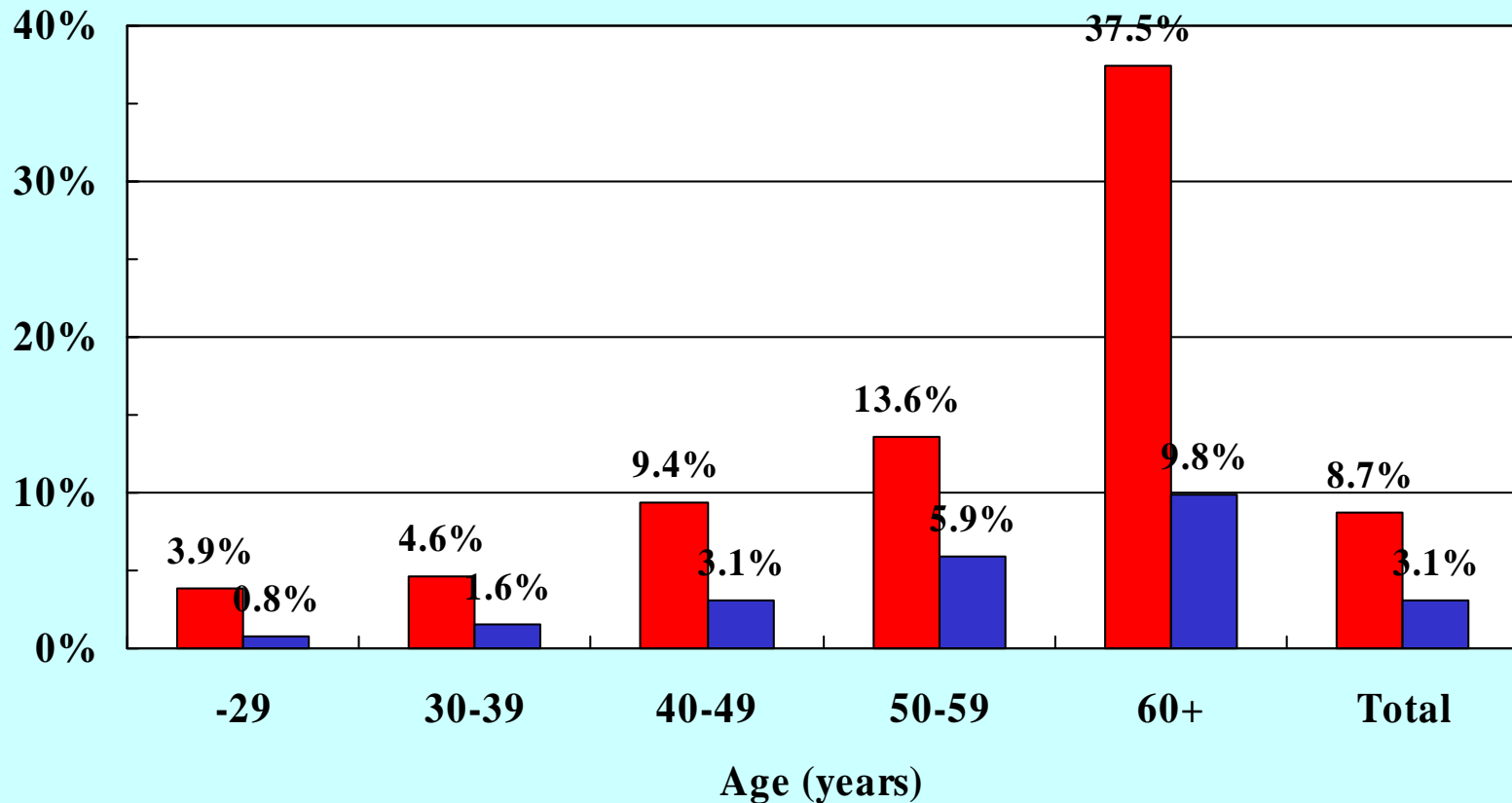
(A Hospital vs Respir Med Hospital)



Respir Med Hospital: Fukujuji Hospital, Japan Anti-TB Association, with a total of 340 beds, 60 for TB, located in Tokyo

Age-specific QFT-G Positivity

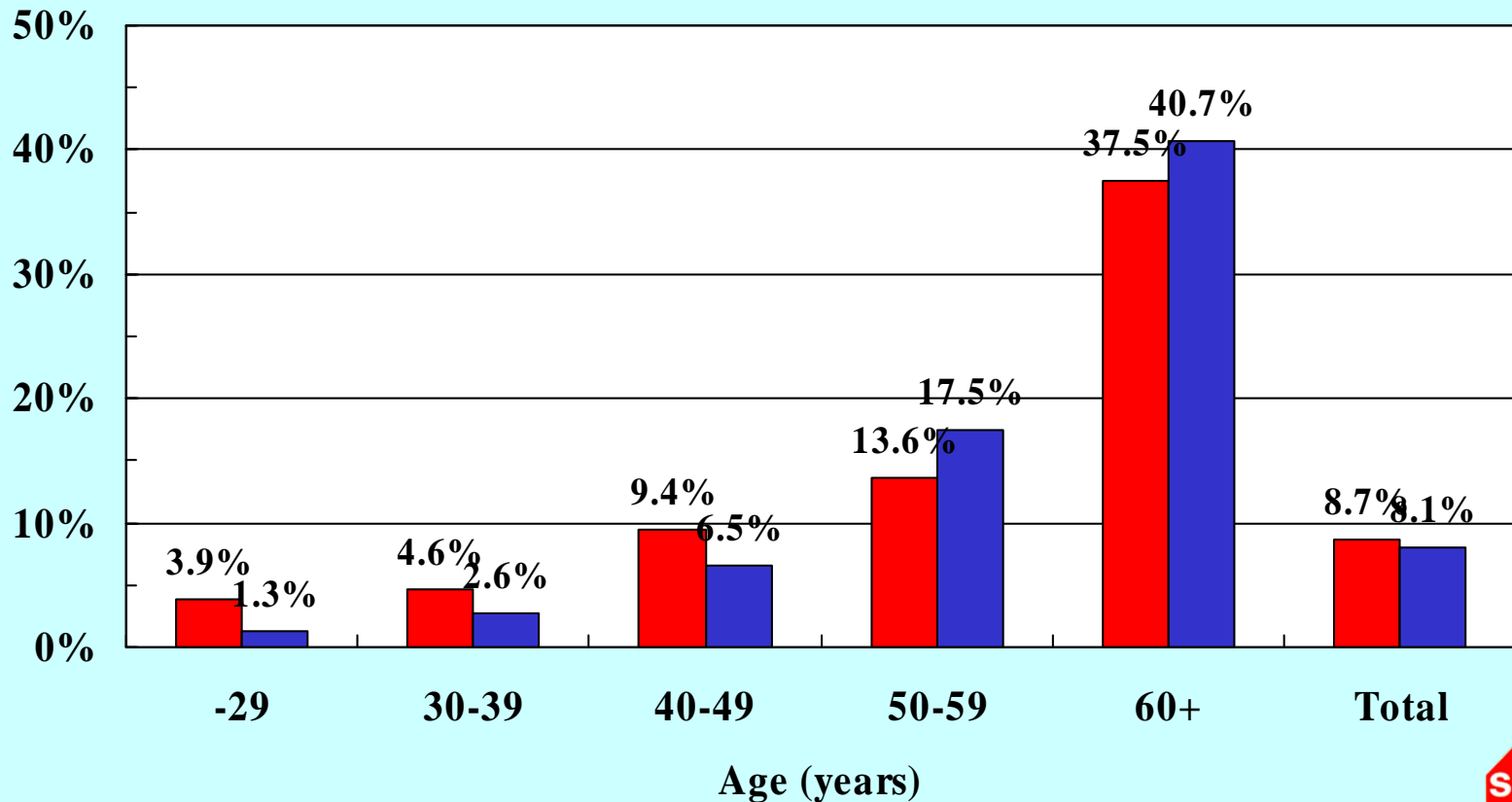
(HCWs vs General Population)



General population: Rate for “-29” was observed in university students, for “30-39” in a company’s employees, and rates for “40+” in a community population.

Age-specific QFT-G Positivity

(HCWs vs Estimated Prevalence of Infection)



QFT-positivity by subject characteristics

		Number	QFT-positive	Adjusted OR	Significance
Total		391	33 (8.4%)		
Sex	Male	102	9 (8.8)	1.5397	0.3747
	Female	289	24 (8.3)	1	
Age	-34 yrs	143	5 (3.5)	1	0.0122
	35-49 yrs	135	11 (8.1)	1.9524	
	50 yrs +	113	17 (15.0)	3.8119	
Job	Doctor	31	1 (3.2)	0.5119	0.6028
	Nurse	183	18 (9.8)	1.9129	
	Technicians	36	4 (11.1)	2.2223	
	Laborers	86	8 (9.3)	1.7219	
	Clerical	55	2 (3.6)	1	
Exposure	TB ward	54	8 (14.8)	1.3162	0.6408
	Emergency room	29	3 (10.3)	1.5890	
	Others	308	22 (7.1)	1	
History	TB/LTBI	21	4 (19.0)	1.5711	0.4924
	None	370	29 (7.8)	1	

New Guidelines for HCWs

(Jap. Soc. TB, Proposed 2009)

- On employment
 - QFT-G to all, or to TST (+)
 - LTBI Rx to QFT-G (+)
- Periodically
 - Chest X-ray (Annual, mandatory)
 - QFT-G in TB Ward/High Risk Workplace Staff
- Contact action
 - QFT-G to all Contacts
 - No follow-up of QFT(-) workers (??)



Questions to be answered

- Risk of Clinical Development: LTBI treatment
 - Recent QFT conversion, with high/low response
 - Other QFT (+)
 - QFT (-), but with healed X-ray lesion
 - QFT (-), but TST (+)
- Contact action
 - Follow-up QFT test to initially QFT (-)
- Cost considerations
 - Universal pre-employment QFT, vs any Combination with TST
 - No pre-employment test
- Specificity & Sensitivity Issues
 - BCG policy change recent and in future





Collaborators

- Dr Harada N (Research Inst. TB)
- Dr Higuchi K (Research Inst. TB)
- Ms Taira S (Miyako HC, Okinawa Pref.)
- Ms Yamauchi Y (Research Inst. TB)

Japan: JST Guidelines 2006: QFT-2G

- Children < 5 y: QFT **useful as an adjunct of active TB Dx, but** not recommended [TST preferred] **for LTBI diagnosis**
- Contacts:
 - Less than 5 years old: TST is preferred over QFT.
 - From 5 to 12 years old: Use QFT with considering use of TST together. The QFT results should be interpreted carefully.
 - From 12 to 18 years: QFT is preferred over TST where QFT test is available. Use TST if necessary.
 - From 18 to 49 years old: QFT is preferred over TST.
 - Over 50 years old: Limited use of QFT/TST. **(usually detection of infection is not prioritized)** --- The "old" infections are supposed to be common (>30%).
- HCWs: QFT preferred over TST
- Active TB: adjunct (supporting) evidence
- High risk groups (diabetes, steroids, TNF-a blockers): QFT is preferred and can be used for deciding on LTBI treatment
- **Even when QFT is preferred, TST may be done first, to be followed by QFT only in those with TST > (e.g.) 10mm diameter, in order to limit the eligible of QFT for cost saving. This is practiced especially in case of mass examination.**

QFT-G In Tube approved in 2009

QFT-G Results in Child TB Patients

(Takamatsu et al, 2007)



	QFT-G Results				
	Pos.	Doubt.	Neg.	Indet.	Total
Bacteriology	14 93%	1 7%	-	-	15
Clinical	14 93%	-	1	-	15
Suspect	1 20%	-	4	-	5
Total	29 83%	1 3%	5 14%	-	35

QFT Findings in Infants (BCG-unvaccinated)

- Of 4 babies (aged 0 – 6 years) with TST (+) , only 2 were QFT-G (+).
- Case 1
 - Mother developed TB SS+, when the baby was 2 mos after birth. TST(-) and QFT(Ind). INH was introduced.
 - 7 mos later TST(+), QFT(Ind)
- Case 2
 - Mother developed TB ss+, when the baby was 1 mo after birth.
 - At 3 mos; TST (+) , QFT(-)
 - AT 7 mos; Still QFT (-)





QFT-G Positivity by TST and Age

(Contacts, BCG-vaccinated)

Erythema	0 yr	1-2 yrs	3-6 yrs	7-12 yrs	13-15 yrs	QFT(+)/Total
$\geq 40\text{mm}$	0/1	0	4/4	3/3	4/4	11/12 92
39-30	0/1	0/3	1/4	2/6	1/1	4/15 27
29-20	0/4	1/4	2/7	0/3	0/1	3/19 16
19-10	0/1	1/5	0/7	0/7	0/1	1/21 5
9-0	0	0/2	0/1	0	0	0/3 0
QFT(+)/Total	0/7 0	2/4 14	7/23 30	5/19 26	5/7 71	19/70 27

(Takamatsu et al, 2008)