

Transmission of MDR/XDR Tuberculosis in Shanghai

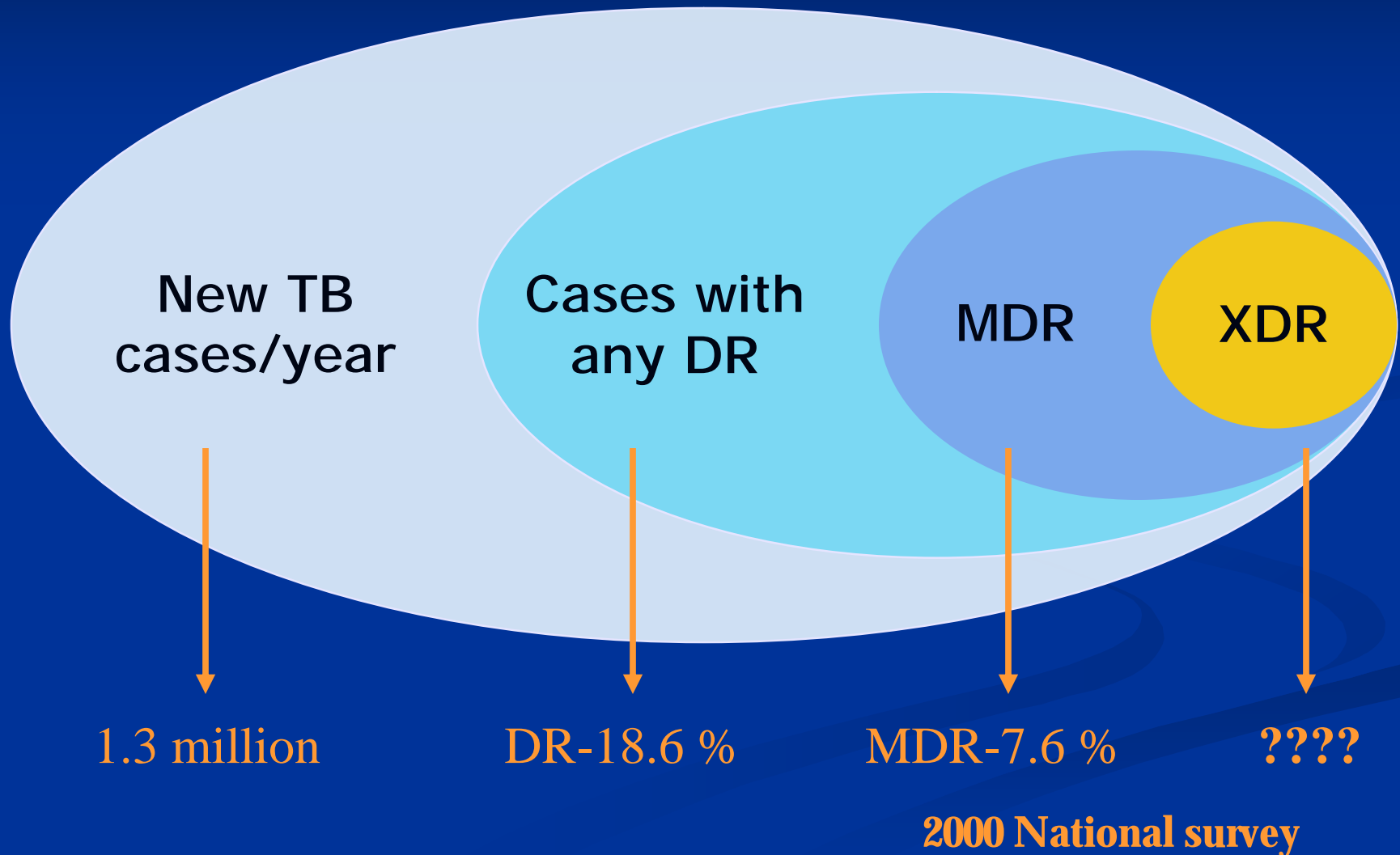
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Drug Resistant TB in China

The Highest DR-TB Burden Country



Objective

- n Whether XDR-TB existed in Shanghai?
- n The rate of XDR-TB among MDR-TB patients?
- n Where did MDR/XDR-TB come from?

Study Design

- n Population: TB patients in Shanghai, 2004-2007
- n DST: Proportion method be used,

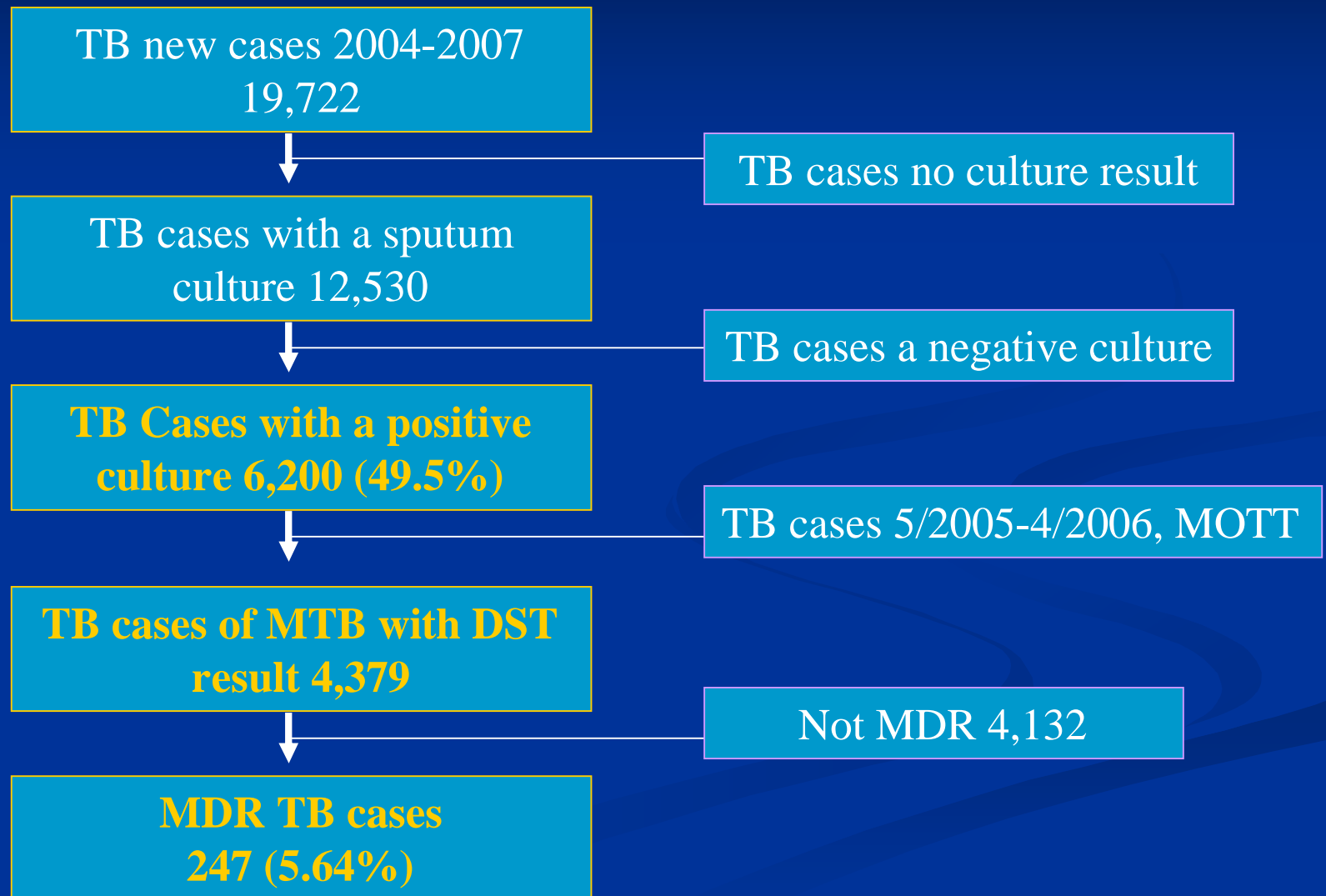
isoniazid (0.2 μ g/ml)
rifampin (40.0 μ g/ml)
streptomycin (4.0 μ g/ml)
ethambutol (2.0 μ g/ml)

ofloxacin (2.0 μ g/ml),
kanamycin (30.0 μ g/ml),
capreomycin (40.0 μ g/ml),
amikacin (40.0 μ g/ml)
4-aminosalicylic acid (1.0 μ g/ml)

Definition

- n **MDR TB.** Resistant to at least INH and RFP
- n **XDR TB.** Resistance to at least INH, RFP, a FQ and one of three injectable second-line drugs
- n **Pre-XDR TB.** Resistant to INH and RFP and either a FQ or a second-line injectable drug, but not both.
- n **Simple MDR TB.** Resistant to just INH and RFP but not pre-XDR TB and XDR-TB.

Patients Selection



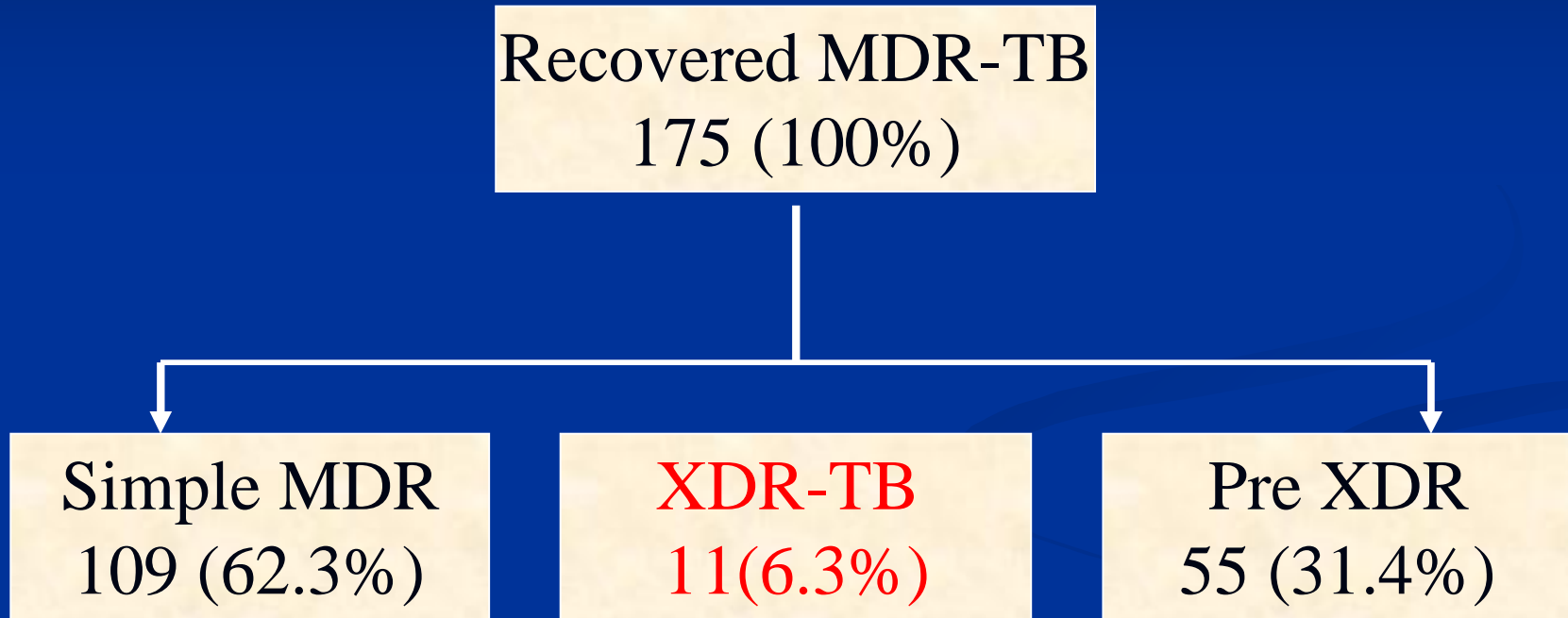
XDR in Shanghai

Recovered MDR-TB
175 (100%)

Simple MDR
109 (62.3%)

XDR-TB
11 (6.3%)

Pre XDR
55 (31.4%)



Case Characteristics

	Total	Simple MDR	Pre-XDR	XDR
Characteristic	n = 175 (%)	n = 109 (%)	n = 55 (%)	n = 11 (%)
Age (years)				
15-29	35 (20.0)	24 (22.0)	11 (20.0)	0 (0)
30-44	53 (30.3)	37 (33.9)	13 (23.6)	3 (27.3)
45-59	57 (32.6)	26 (23.9)	23 (41.8)	8 (72.7)
60-74	20 (11.4)	14 (12.8)	6 (10.9)	0 (0)
≥75	10 (5.7)	8 (7.4)	2 (3.6)	0 (0)
Treatment				
New	105 (60.0)	69 (63.3)	30 (54.5)	6 (54.5)
Treated	70 (40.0)	40 (36.7)	25 (45.5)	5 (45.5)

MDR/XDR in China

- n Beijing Chest Hospital, 2002.01-2005.12,
 - n INH, RFP, SM, EMB, AmK, OFX, PZA, ETH, PAS (9 drugs)
 - n 10.75% (207/1926) MDR, 6.28% (13/207) XDR

J. Clin. Microbiol. doi:10.1128/JCM.00822-08

- n Beijing Tuberculosis & Thoracic Tumor Research Institute, 1998.06-2006.03
 - n INH, RFP, SM, EMB, KM, CPM, AK, 1321Th, PAS, OFX, LFX, RIFT (12 drugs)
 - n 34.8% (673/1934) MDR
 - n 67 MDR, 22 XDR, 15 TDR (more than 24 months in the Institute treated patients)

The Journal of the Chinese Antituberculosis Association, 2008, 30 (2):113-117

MDR/XDR Epidemic

- n Where did the MDR/XDR come from?
 - n Treated cases: acquired drug resistance
 - n Poor Patient Management
 - NEED BETTER PATIENT CARE**
 - n New cases: primary drug resistance (>50%)
 - n Transmission of drug resistant TB
 - NEED BETTER TB CONTROL**

Is the Required DR Really Required?

Mechanism

Vs.

Surveillance

Primary

=

No Prior Therapy

Acquired
(Gene mutation
on one strain)

~~=~~

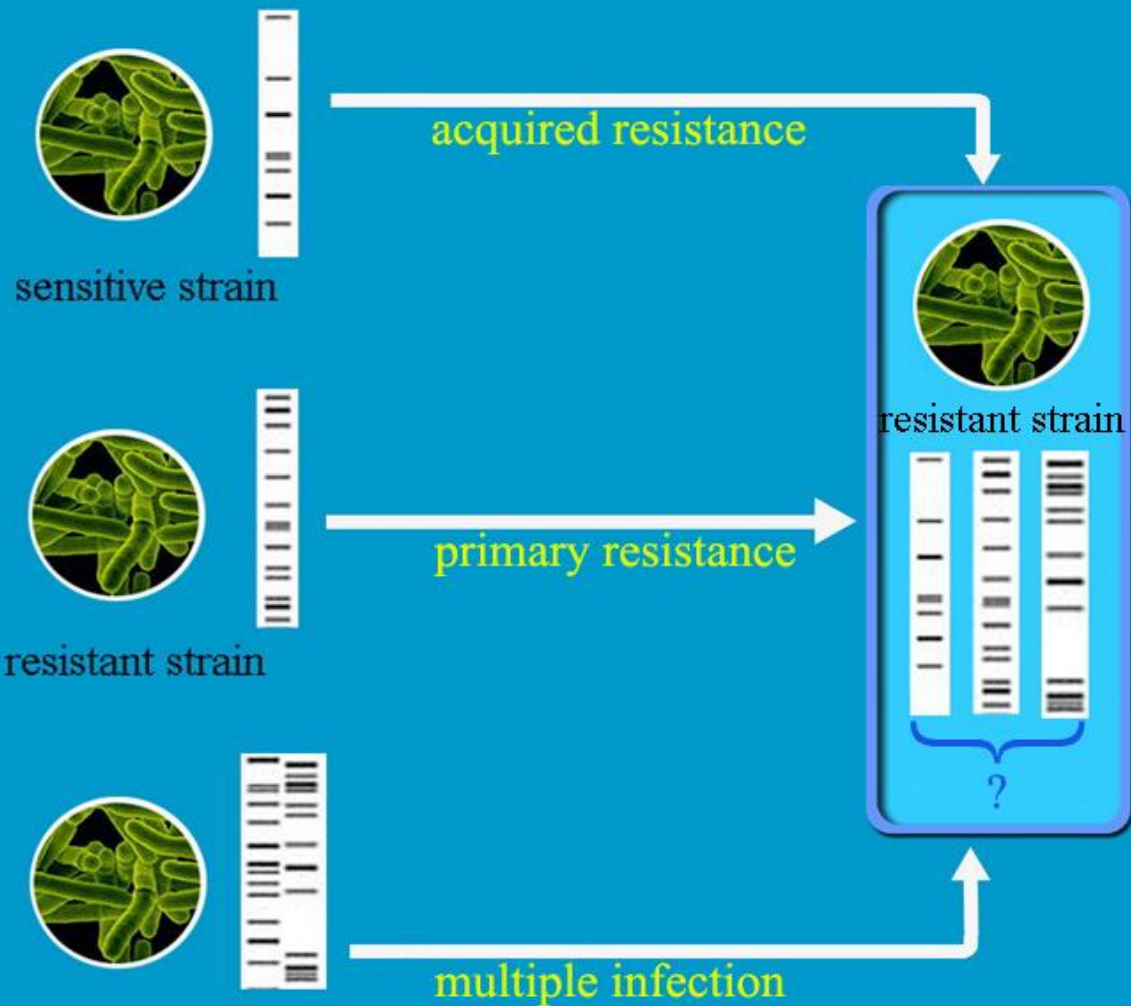
Currently or
Previously Treated

Some previously treated
patients can be reinfected

Study Objective

To investigate the cause of drug resistance among treated patients, using genotyping techniques

Research Hypothesis



Specimen Collection

- n Case definition of treated patients
 - n Patients with recurrent tuberculosis
 - n Patients still under treatment
- n Criteria for specimens
 - n Isolates from 1999-2004, stored at Shanghai CDC
 - n Two or more isolates with different drug susceptibility test results were collected from individual treated patients

Sampling Frame

TB patients, 1999 to 2004: 6,622

TB patients with discordant drug susceptibility test results: 100

Both isolates have genotype results: 38

Second isolate was drug susceptible or resistant to fewer drugs: 6

Second isolate resistant to more drugs: 32

Genotyping Methods

- n MIRU typing for all isolates
- n IS6110-RFLP typing for isolates with identical MIRU patterns
- n Classification of drug resistance
 - n Acquired drug resistance: identical MIRU and RFLP patterns
 - n Primary drug resistance: different MIRU or RFLP patterns

Results

- n Among total 32 patients, 27 (84%) patients had a pair of isolates with discordant MIRU or RFLP patterns
- n 5 patients (16%) had a pair of isolates with identical MIRU and RFLP patterns
- n Among treated patients, 84% DR were due to primary drug resistance.

Li X *et al.* JID 2007, 195: 864-869

Conclusion

- n 5.6% of the TB cases were MDR, and 6.3% of the MDR TB were actually XDR in Shanghai.
- n >50% MDR / XDR TB patients were new cases.
- n Among treated patients, 84% DR were due to primary drug resistance.
- n **Ongoing transmission of MDR/XDR is a serious problem in Shanghai, probably in China too. New strategies to block the transmission of MDR/XDR-TB are urgently needed**

Acknowledgment

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Thank you!