The current antimicrobial susceptibility in *Chlamydia trachomatis* in Japan from the nationwide surveillance

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Background

Chlamydia trachomatis is one of the principal pathogens for non-gonococcal urethritis (NGU). There have been a few studies about the novel resistant strains isolated from the patients with genital chlamydial infection. However, current common concept showed that those were the temporary and unstable strains with decreased antimicrobial susceptibility (ref. 1). On the other hand, the reduced susceptibility to levofloxacin or azithromycin in *Mycoplasma genitalium*, one of pathogens of NGU, has been intensively studied in Europe and Japan.

Purpose

In the three societies as Japanese Society of Chemotherapy, Japanese Association of Infectious Diseases and Japanese Society of Clinical Microbiology tried to perform the first national surveillance for *C. trachomatis* between April 2009 and October 2010. Base on this data, the current situation of antimicrobial susceptibility in *C. trachomatis* is discussed.

Results

From 28 facilities, 207 specimens were collected and sent to KURC.
Forty eight specimens were positive for *C. trachomatis* by culture.
In these specimens, antimicrobial susceptibility testing could be performed in 19 strains. The findings of urethral discharge in 48 patients and the results of susceptibility testing were shown below. The clinical findings were mostly common to the previous reports (ref. 3).
The median age of these 48 patients was 31 years (range; 17 to 71).

Qualitative findings	
Clear	43 (90.0%)
Purulent	4 (8.3%)

The record of one patient was not described.

Quantitative findings	
None	1 (0.2%)
Scanty	33 (68.8%)
Moderate	10 (20.8%)
Profuse	4 (8.3%)

Materials and methods

Study design; Prospective study as nationwide surveillance.

Patients; Heterosexual male patients with NGU who were 16 years old or older from Apr/2009 to Oct/2010 in 51 medical facilities in 8 prefectures of Japan.

Specimens collection; the specimens of urethral swab were collected from the patients. The specimens were sent to Kitasato University Research Center (KURC) for Anti-infectious Drugs by using BD Universal Viral Transport.

Susceptibility testing and MIC determination; The measurement of antimicrobial susceptibilities were performed according to the standard method of Japan Society of Chemotherapy (ref. 2). The method is based on the determination of the minimum drug concentration which completely inhibits the formation of chlamydial inclusions in HeLa 229 cells cultures *in vitro*. The drugs for antimicrobial susceptibility testing were shown below.

Clinical findings; The quality and quantity of urethral pus discharge were recorded (ref. 3). In the qualitative findings, **clear** means mucoid, translucent, and no discoloration. **Purulent** means opalescent, and whitish or yellow to green. In the quantitative findings, **scanty** means a small quantity of discharge only on stripping the urethra. **Moderate** means a large quantity of discharge on stripping the urethra. **Profuse** means discharge spontaneously dripping from the external urethral meatus.

Ethical considerations

The details of this research project were approved the Review Board in Sapporo Medical University Hospital (No. 20-80) and written informed consent was obtained from each subject.

abbreviation	Antimicrobial agents
LVFX	levofloxacin
CPFX	ciprofloxacin
TFLX	tosufloxacin
STFX	sitafloxacin
EM	erythromycin
CAM	clarithromycin
AZM	azithromycin
MINO	minocycline
DOXY	doxycycline

Antimicrobial agents	Present study				Donati M. et al.	Bébéar CM et al.	Ljubin-Sternak S. et al.
	MIC50	MIC90	MIC (range)	D/UW-3Cx	MIC	MIC	MIC
LVFX	0.25	0.25	0.125-0.5	0.25	0.5	-	-
CPFX	2	4	1-4	1	-	-	-
TFLX	0.125	0.25	0.06-0.125	0.06	-	-	-
STFX	0.06	0.125	0.03-0.25	0.016	-	-	-
EM	0.06	0.25	0.03-0.25	0.125	0.5-1.0	0.015-1	-
CAM	0.008	0.016	<0.004-0.03	0.016	0.015-0.06	-	-
AZM	0.125	0.5	0.125-0.5	0.125	0.25-0.5	0.015-0.5	0.064-0.125
MINO	0.5	1	0.125-2	0.25	-	-	-
DOXY	0.125	0.25	0.03-0.5	0.125	0.03-0.06	0.015-0.5	0.016-0.064

Discussion

In Japan, the current standard treatment regimens are still effective for patients with chlamydial urethritis and no resistant strains were detected in this surveillance.
AZM, one of the recommended treatment regimens, remained effective in *in vitro* tests and the susceptibility was mostly similar to that reported previously (ref. 4-6).
The susceptibility to tetracycline, including MINO and DOXY, was less favorable than expected. The reason was not clear and we need to determine it in the future.
Recently, the antimicrobial susceptibility of *Mycoplasma genitalium*, one of the pathogens of NGU, has been discussed. A recent report revealed that the clinical efficacy of AZM might be decreased for *M. genitalium*-positive urethritis (ref. 7). For appropriate treatment, because the susceptibility of *M. genitalium* to STFX was higher than to other antimicrobial agents in the previous studies (refs. 8, 9), STFX, a new generation quinolone, is promising for treatment of patients with NGU.

Conclusion

The nationwide surveillance showed that no resistant strains of *C. trachomatis* have been detected in Japan to date.

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