どこからがアブナイ？　病気がうつる性行為とは

感染しやすい＝うつる性行為

- ディープキス（舌を口の中まで入れる）
- 裸で抱き合う、ペッティング
- 膣性交
  - 初めてでない
  - コンドームをしない
- 肛門性交　（アナル）
- 口腔性交（フェラチオ・クンニリングス・リミング）
- 相手のマスターベーションを素手で行う

感染しない＝うつらない性行為

- 軽いキス（頬っぺたや唇の表面にﾁｭｯ）
- 服を着て抱き合う、手をつなぐ
- 膣性交
  - ふたりとも絶対に初めて
  - どちらも性感染症を持ってない

こっち側はセーフ！

- 自分で行うマスターベーション

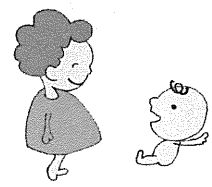
ＨＩＶの感染経路

ＨＩＶ → 性行為＊（膣・ペニス・肛門・口等）→ 感染
ＨＩＶ → 注射の回し打ち・刺青 → 感染
ＨＩＶ → 出産・授乳 → 感染
ＨＩＶ → 輸血・血液製剤（現在、血液製剤は安全です）→ 感染

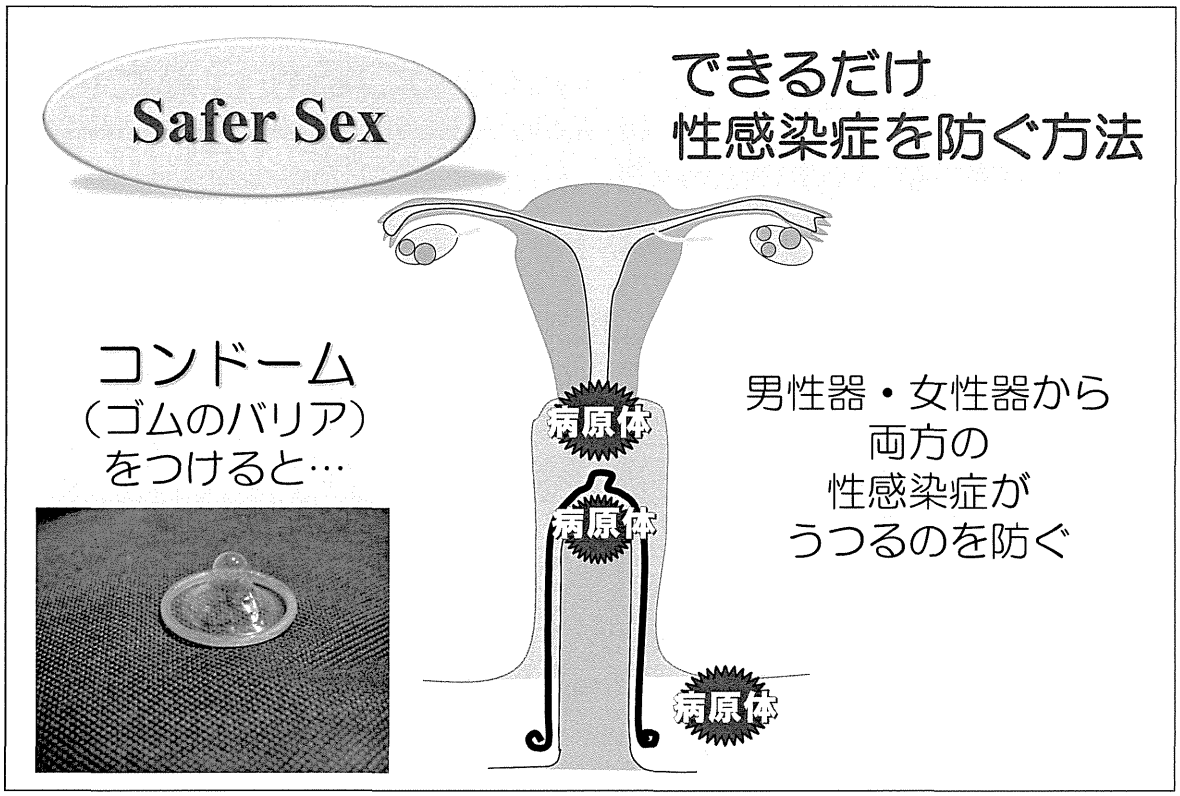
①性行為

②注射の回し打ち

③出産・授乳



＊男性同性間性的接触者での感染が多い

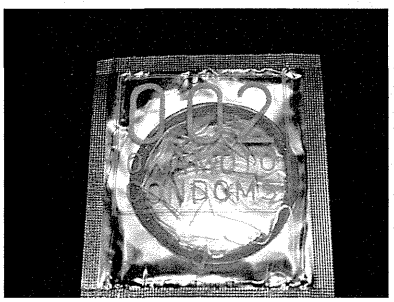


コンドームの常識　　A１～３

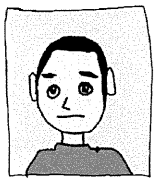
- A１　コンドームは、財布やズボンのポケットに入れてたら傷つきやすいので×
  持ち運びはハードケースにいれる○
- A２　ラブホのコンドームは袋に穴が開いてたり、期限が切れてるかも。信用できないので×
- A３　２枚重ねは、圧がかかって外れやすく、破れやすいので×

では聞きます。

あなたは彼に
コンドームを
つけさせられますか？



幸せになるために　今からできること




- 助けを求める勇気と行動力
（相談・受診する）
- 性のトラブルに責任をもてるまでコンドームを使う
- ワクチンや検査を受ける
- No!と言える自分、No!　と言われてへこまない自分をつくる

・・・考えるのはあなたです。




Ⅲ．研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

〈雑　　誌〉

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Shigemura K, Osawa K, Miura M, Tanaka K, Arakawa S, Shirakawa T, Fujisawa M	Azithromycin resistance and its mechanism in Neisseria gonorrhoeae strains in Hyogo, Japan	Antimicrob Agents Chemother	59(5)	2695-2699	2015
Harnasuna R, Yasuda M, Ishikawa K, Arakawa S, Fujisawa M, et al.	The second nationwide surveillance of the antimicrobial susceptibility of Neisseria gonorroeae from male urethritis in Japan, 2012-2013	J Infect Chemother	21	340-345	2015
谷畑　健生, 秋元　義弘, 武島　　仁, 五十嵐辰男, 安田　　満, 種部　恭子, 金山　博臣, 荒川　創一	平成25年7モデル県の性感染症診療医療機関全数調査推計有病率と国立率感染症研究所の定点報告推計有病率の比較～7県医療機関全数調査結果と定点調査報告結果の有病率はなぜ乖離したのか？	日本性感染症学会誌	26(1)	109-116	2015
中瀬　克己	特定感染症予防指針の変更を踏まえた自治体における性感染症発生動向調査の活用	ニューズレター「性の健康」	Vol.15 No.1	1 - 3	2015
白井　千香, 古林　敬一, 川畑　拓也, 吉田　弘之, 荒川　創一	性感染クリニック及び産科における口腔内性感染症に関するアンケートと検体検査の試み	日本性感染症学会誌	26(1)	91-96	2015
余田　敬子	口腔・咽頭に関連する性感染症	日本耳鼻咽喉科学会会報	118	841-853	2015
余田　敬子	口腔粘膜疾患 —特徴と治療の要点— 性感染症を疑う口腔粘膜疾患の診療	MB ENT	178	62-72	2015
余田　敬子	診断・治療に必要な耳鼻咽喉科臨床検査 —活用のpointとpitfall— 咽喉頭炎の鑑別	MB ENT	179	156-164	2015

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Mikamo H, Matsumizu M, Nakazuru Y, Nagashima M	Efficacy and safety of metronidazole injection for the treatment of infectious peritonitis, abdominal abscess and pelvic inflammatory diseases in Japan.	J Infect Chemother	21	96-104	2015
Mikamo H, Matsumizu M, Nakazuru Y, Okayama A, Nagashima M.	Efficacy and safety of a single oral 150 mg dose of fluconazole for the treatment of vulvovaginal candidiasis in Japan.	J Infect Chemother	21	520-526	2015
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Matsumoto K, Maeda H, Oki A, Takatsuka N, Yasugi T, Furuta R, Hirata R, Mitsuhashi A, Kawana K, Fujii T, Iwata T, Hirai Y, Yokoyama M, Yaegashi N, Watanabe Y, Nagai Y, Yoshikawa H	Human leukocyte antigen class II DRB1*1302 allele protects against cervical cancer: at which step of multistage carcinogenesis?	*Cancer Sci*, doi: 10.1111/cas.12760	106	1448	2015
Seiki T, Nagasaka K, Kranjec C, Kawana K, Maeda D, Taguchi A, Wada-Hiraike O, Oda K, Nakagawa S, Yano T, Fukayama M, Banks L, Osuga Y, Fujii T	HPV-16 E6 impairs the subcellular distribution and levels of expression of protein phosphatase 1γ in cervical malignancy	*BMC Cancer*	15	230	2015

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著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
荒川　創一	グラム陰性球菌感染症 Ⅰ髄膜炎菌感染症 Ⅱ淋菌感染症	井村　裕夫	わかりやすい内科学 第４版	文光堂		2014	394-395
三鴨　廣繁	淋菌感染症		今日の小児治療指針 第16版	医学書院	東京	2015	382-383

Ⅳ．研究成果の刊行物・別刷

AAC
Journals.ASM.org

Azithromycin Resistance and Its Mechanism in *Neisseria gonorrhoeae* Strains in Hyogo, Japan

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Therapeutic options are limited for *Neisseria gonorrhoeae* infection, especially for oral drugs. The purpose of this study was to investigate the susceptibility of *N. gonorrhoeae* to oral azithromycin (AZM) and the correlation between AZM resistance-related gene mutations and MIC. We examined the AZM MICs of clinical strains of *N. gonorrhoeae*, sequenced the peptidyltransferase loop in domain V of 23S rRNA, and investigated the statistical correlation between AZM MIC and the presence and number of the mutations. Among 59 *N. gonorrhoeae* strains, our statistical data showed that a deletion mutation was seen significantly more often in the higher-MIC group (0.5 μg/ml or higher) (35/37; 94.6%) than in the lower-MIC group (0.25 μg/ml or less) (4/22; 18.2%) ($P < 0.0001$). However, a mutation of codon 40 (Ala→Asp) in the *mtrR* gene (helix-turn-helix) was seen significantly more often in the lower-MIC group (12/22; 54.5%) ($P < 0.0001$). In *N. gonorrhoeae* multiantigen sequence typing (NG-MAST) analyses, ST4777 was representative of the lower-MIC group and ST1407, ST6798, and ST6800 were representative of the higher-MIC group. NG-MAST type 1407 was detected as the most prevalent type in AZM-resistant or -intermediate strains, as previously described. In conclusion, a deletion mutation in the *mtrR* promoter region may be a significant indicator for higher MIC (0.5 μg/ml or higher). ST4777 was often seen in the lower-MIC group, and ST1407, ST6798, and ST6800 were characteristic of the higher-MIC group. Further research with a greater number of strains would help elucidate the mechanism of AZM resistance in *N. gonorrhoeae* infection.

Neisseria gonorrhoeae infection is often seen in male urethritis and female cervicitis, and its diagnosis has historically led to prompt initiation of treatments with a single antibiotic (1, 2). In the 1990s in most Asian countries, fluoroquinolones (FQs) were often used for this infection, partly because FQs have higher concentrations in the urinary tract. FQs showed good initial outcomes for this infection, but the results were not enduring. This may be partly due to the trend for single use of FQs for this infection, with no guidelines to recommend other choices (3–9).

In addition to the FQs, cephalosporins such as cefixime were also recommended as oral antibiotics until these drugs showed decreased activity against *N. gonorrhoeae* (10). They are no longer a recommended choice for this infection (11–13). Oral antibiotics for outpatient treatment would be highly desirable for this kind of infection. Azithromycin (AZM) is an oral antibiotic with medical insurance approval for use against chlamydia infections (14), and there are many reports of good activity against *N. gonorrhoeae* infection (15). Other reports suggest that *N. gonorrhoeae* infection is less susceptible to AZM and that AZM-resistant strains have emerged (5). We investigated the AZM susceptibilities of *N. gonorrhoeae* strains and the correlation between mutations of macrolide resistance-related genes and the AZM MICs of clinically isolated strains of *N. gonorrhoeae*.

Three mechanisms of resistance to AZM are known: overexpression of the efflux pump, mutation in the peptidyltransferase loop in domain V of 23S rRNA, and modification of the ribosomal target by methylase. Macrolides such as AZM and erythromycin (EM) bind to 4 alleles of the 23S rRNA component of the 50S subunit of the bacterial ribosome and restrain protein synthesis by inhibiting the elongation of peptide chains (16).

Overexpression of the MtrCDE pump is due to either the lack of repressor MtrR protein, which occurs by a single-base-pair deletion or TT insertion in the promoter region, or missense mutations in the *mtrR* coding region (17). Modification of the ribosomal target by methylase or mutations reduces the affinity of the macrolide antibiotics for ribosomes (18). Since the use of antimicrobial agents for treatment of gonococcal infections is different in each country, the trend of drug resistance in gonococci is likely different geographically (19). Hence, epidemiological investigations should be done in each country. Previous studies have reported a high use of *N. gonorrhoeae* multiantigen sequence typing (NG-MAST), which is based on limited DNA sequence analyses of two highly polymorphic loci, *porB* and *tbpB*, in sequence type (ST) 1407 *N. gonorrhoeae*, which is multidrug resistant and appears to be disseminated basically worldwide (20). The selection and spread of AZM resistance are driven by inappropriate treatment of patients with suboptimal doses of AZM for gonococcal infection. *N. gonorrhoeae* maintains its genetic resistance determinants even after the removal of antibiotic selection pressure.

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doi:10.1128/AAC.04320-14

TABLE 1 Sequences for PCR primers for azithromycin resistance genes

Primer name	Target gene	Primer sequence (5′ to 3′)	Size (bp)	Reference
gonoRNA-F	23S rRNA	ACGAATGGCGTAACGATGGCCACA		
allele1		TCAGAATGCCACAGCTTACAAACT	2,054	16
allele2		GCGACCATACCAAACACCCACAGG	2,240	
allele3		GATCCCGTTGCAGTGAAGAAAGTC	2,217	
allele4		AACAGACTTACTATCCCATTCAGC	1,847	
mtrF1	*mtrR*	GCCAATCAACAGGCATTCTTA	380	17
mtr13Ra		GTTGGAACAACGCGTCAAAC		
ermA-F	*ermA*	CTTCGATAGTTTATTAATATTAGT	645	18, 21, 22
ermA-R		TCTAAAAAGCATGTAAAAGAA		
ermB-F	*ermB*	AGTAACGGTACTTAAATTGTTTAC	639	
ermB-R		GAAAAGGTACTCAACCAAATA		
ermC-F	*ermC*	GCTAATATTGTTTAAATCGTCAAT	642	
ermC-R		TCAAAACATAATATAGATAAA		
ermF-F	*ermF*	CGGGTCAGCACTTTACTATTG	466	
ermF-R		GGACCTACCTCATAGACAAG		

Surveillance and characterization of the mechanisms of AZM resistance are essential. In this study, we investigated the genetic characteristics of *N. gonorrhoeae* strains with decreased susceptibility to AZM.

MATERIALS AND METHODS

Strains. *N. gonorrhoeae* strains were isolated from patients with male urethritis or female cervicitis and sent to Hyogo Rinsho Co. Ltd., Himeji, Japan. Gonococcal strains were retrieved from storage at −80°C by 48 h of incubation (35°C, 5% CO_2) on chocolate agar. The resulting colonies were then subcultured.

MIC measurements. The MIC (μg/ml) was determined using an Optopanel E212 dry plate (Kyokuto Pharmaceutical Industrial Co., Ltd., Tokyo, Japan) with the broth microdilution method. For AZM, the MIC breakpoints from the European Committee on Antimicrobial Susceptibility Testing (EUCAST) were used (http://www.eucast.org). For quality control, the *N. gonorrhoeae* reference strain ATCC 49226 was included in each testing.

DNA extraction. DNA extracts were suspended in 500 μl of Tris-EDTA (TE) buffer for 10 min and then boiled for 15 min and centrifuged at 15,000 rpm for 10 min. The final supernatant was retained for storage at −20°C.

PCR amplification and sequencing of AZM resistance genes. To examine the mutations in the peptidyltransferase loop of domain V of the 23S rRNA gene, containing four copies, all four alleles were amplified by PCR and sequencing as described previously (16). The *mtrR* promoter region was examined by PCR and sequencing as described previously (17). DNA sequencing was performed after the PCR using PCR amplicons. Purification of the PCR products was performed with the QIAquick PCR purification kit (Qiagen, Hilden, Germany), and the sequencing was performed at Eurofins Genomics, Inc. (Tokyo, Japan) (Table 1).

PCR of the *erm* genes. The methylase genes *ermA*, *ermB*, *ermC*, and *ermF* were detected using PCR with primers and conditions as described previously (18, 21, 22). The PCR primers are shown in Table 1. The PCR conditions were as follows: denaturing at 94°C for 30 s; annealing at 50°C for 30 s (*ermB* and *ermF*), 48°C for 1 min (*ermA*), or 43°C for 1 min (*ermC*); and elongation at 72°C for 2 min. The cycle was repeated 35 times (18, 21, 22).

Molecular epidemiological typing. NG-MAST was performed by using PCR and sequencing of the more variable segments of *porB* and *tbpB* (23). The *porB* and *tbpB* allele numbers as well as NG-MAST STs were assigned using the NG-MAST website (http://www.ng-mast.net/).

Statistical analyses. We investigated the statistical correlation between the AZM MIC and the presence and number of mutations under the classifications of an MIC of 0.25 μg/ml or less (lower-MIC group) and 0.5 μg/ml or higher (higher-MIC group). Statistical analysis was conducted using Fisher's exact test with the JSTAT (Java Virtual Machine Statistics Monitoring Tool; Sun Microsystems, Inc., Santa Clara, CA). Statistical significance was established at a P value of 0.05.

RESULTS

AZM MICs. The AZM MICs of the 59 strains collected were 0.06, 0.12, 0.25, 0.5, 1, and 16 μg/ml. In detail, 2 strains (3.39%) had an MIC of 0.06 μg/ml, 5 strains (8.47%) had an MIC of 0.12 μg/ml, 16 strains (27.1%) had an MIC of 0.25 μg/ml, 33 strains (55.9%) had an MIC of 0.5 μg/ml, 4 strains (6.78%) had an MIC of 1 μg/ml, and 1 strain (1.69%) had an MIC of 16 μg/ml. The MIC_{50} was 0.5 μg/ml, and the MIC_{90} was 0.5 μg/ml (Table 2).

Mutations in domain V of 23S rRNA. There were 2 strains with C2214T (C204T) mutations in allele 3, one strain with a G2209A (G199A) mutation in allele 4 and one strain (with the highest MIC, 16 μg/ml) with C2599T (C589T) mutations in all 4 alleles in the peptidyltransferase loop in domain V of 23S rRNA.

***mtrR* mutations.** There were 38 (64.4%) strains with an A deletion mutation in the promoter region of *mtrR*, and this was seen significantly more often in the higher-MIC group (0.5 μg/ml or higher) (35/37; 94.6%) than the lower-MIC group (0.25 μg/ml or less) (4/22; 18.2%) ($P < 0.0001$). Conversely, mutations of codon 40 (Ala→Asp) in the *mtrR* gene (helix-turn-helix) were seen significantly more often in the lower-MIC group (12/22; 54.5%) ($P < 0.0001$). In addition, except for deletion mutations, strains with no mutation were seen significantly more often in the higher-MIC group (33/37; 89.2%) ($P < 0.0001$), and strains with one mutation were seen significantly more often in the lower-MIC group (15/22; 68.2%) ($P < 0.0001$).

Detection of methylase genes. Of the 59 *N. gonorrhoeae* strains, there were no strains with positive PCR detection of *ermA*, *ermB*, *ermC*, or *ermF* (data not shown).

NG-MAST. *N. gonorrhoeae* multiantigen sequence typing (NG-MAST) results for *porB* and *tbpB* classified the 59 *N. gonorrhoeae* strains as ST3505, ST4015, ST4637, ST4777, ST5875, ST6761, ST6773, ST6775, ST7382, and ST7806 in the lower-MIC group and ST247, ST1407, ST3520, ST3588, ST4044, ST4163, ST4186, ST5875, ST6764, ST6774, ST6798, and ST6800 in the higher-MIC group. The highest MIC in our strains (16 μg/ml) was found for ST1407. ST4777 was representative of the lower-MIC

TABLE 2 MICs, mutations, and NG-MAST results for the *N. gonorrhoeae* strains

AZM MIC	No. of strains	% of strains	Mutations[a]							NG-MAST type(s) (no. of strains)
			mtrR promoter region		*mtrR* gene					
					Helix-turn-helix					
			A deletion	C→T mutation	Codon 39 (Ala→Thr)	Codon 40 (Ala→Asp)	Codon 45 (Gly→Asp)	Codon 29 (silent mutation)	Codon 30 (silent mutation)	
16	1	100	×							ST1407 (1)
1	4	100	×							ST6798 (3), ST1407 (1)
0.5	28	88	×							ST1407 (5), ST6800 (5), ST6798 (2), ST4044 (2), ST3588 (2), ST247 (1), ST3520 (1), ST4163 (1), ST4186 (1), ST5875 (1), ST6764 (1), ST6774 (1), nontypeable (9)
	2	6	×				×			
	1	3		×	×			×	×	
	1	3					×			
0.25	8	50				×				ST4777 (2), ST6761 (2), ST6775 (2), ST4015 (1), ST4637 (1), ST5875 (1), ST7382 (1), ST7806 (1), nontypeable (5)
	3	19		×	×			×	×	
	2	13	ND	ND	ND	ND	ND	ND	ND	
	1	6	×							
	1	6					×			
	1[b]	6								
0.125	4	100				×				ST4777 (1), ST6773 (1), nontypeable (2)
0.06	2	100	×				×			ST3505 (1), nontypeable (1)
Total	59									

[a] ×, mutation present; ND, not determined.
[b] 100-bp insertion and mutation.

group, and ST1407, ST6798, and ST6800 were representative of the higher-MIC group (Table 2).

DISCUSSION

The mechanism of resistance for the AZM-resistant *N. gonorrhoeae* phenotype is currently unknown in detail. AZM and other macrolides exert a bacteriostatic effect by interacting directly with the central loop of domain V, the site of peptide bond formation, thereby inhibiting protein synthesis. Alteration in 23S rRNA is reported to contribute to low-level resistance. A 23S rRNA mutation (C2611T) has been proposed to contribute to the low-level resistance observed in two Canadian gonococcal strains (24). Chisholm et al. showed that very-high-level resistance to AZM (MIC, 256 μg/ml) occurs in *N. gonorrhoeae* as a result of a single point mutation in the peptidyltransferase region of domain V of the 23S rRNA gene (24). Our study included a high-level AZM-resistant strain (MIC, 16 μg/ml) with C2599T mutations in all the alleles (alleles 1 to 4) tested. This suggests that gonococcal strains from Japan may have more mutations, even in strains with lower MICs, than those from other countries, such as the United Kingdom.

We observed that all AZM-resistant strains contained several mutated alleles and that highly resistant strains had at least 3 mutations, while sensitive and moderately resistant isolates had a maximum of one mutated allele. Mutation of A2059G in highly resistant gonococci and C2611T mutations in the 23S rRNAs of moderately resistant gonococci were reported previously (16). Our study found strains with mutations in one allele even in strains with low MICs (0.25 to 0.50 μg/ml), indicating that even gonococci with comparatively lower MICs harbor mutations.

Another mechanism of AZM resistance, the efflux pump, is well known to contribute to macrolide resistance. This pump excretes antibiotics, resulting in insufficient intracellular accumulation. The MtrCDE efflux pump regulated by the MtrR repressor protein is a representative efflux pump system. *mtrR* mutations in the gene itself or in its promoter region have been reported in low-level macrolide-resistant gonococcal strains (25, 26) because of decreased MtrR expression and upregulation of the MtrCDE efflux pump. Clinical isolates or laboratory-derived mutants that display resistance to hydrophobic agents frequently contain loss-of-function mutations in the *mtrR* coding sequence or a single-base-pair deletion in a 13-bp inverted repeat within the *mtrR* promoter (27–29).

The *mtrR* mutations in the clinical isolates described above were identical to those reported for other strains of gonococci that express resistance to multiple hydrophobic compounds (30, 31). The combined genetic and molecular results obtained in this investigation implicate the *mtrCDE*-encoded efflux pump as a mechanism by which gonococci can express decreased susceptibility to AZM. Through known mutations (27) that abrogate transcription of the gene (*mtrR*) that encodes a transcriptional repressor of *mtrCDE* or loss-of-function mutations in the repressor-encoding gene, gonococci can overproduce the MtrCDE efflux pump to increase their capacity to export hydrophobic agents. Our data showed that a deletion mutation in the promoter region of *mtrR* was seen significantly more often in the higher-MIC group (0.5 μg/ml or higher) compared with the lower-MIC group (0.25 μg/ml or less) ($P < 0.0001$), and conversely, a mutation of codon 40 (Ala→Asp) in the *mtrR* gene (helix-turn-helix) was seen significantly more often in the lower-MIC group ($P <$

0.0001). These findings contribute to the current understanding of the mechanism of AZM resistance in *N. gonorrhoeae*. However, the methylase genes were not detected in our tested *N. gonorrhoeae* strains, indicating that our AZM-resistant strains did not have the same mechanisms of macrolide resistance as seen in the study by Roberts et al. (18). The trend of AZM resistance has not yet become widespread, and thus we need to continue surveillance of gonococcal sensitivity to AZM but also continue with mechanistic studies.

As an epidemiological study tool, the NG-MAST method (32–36) is based on limited DNA sequence analyses of two highly polymorphic loci, *porB* and *tbpB* (23). There is public Internet access for sequence submission and assignment of sequence types, either for *porB* or *tbpB* or for the assignment of STs using a combination of these two loci (23). Our study clearly showed that STs could be usefully classified according to high-level and low-level AZM MICs. To our knowledge, there is no report of NG-MAST STs and AZM MICs. We identified ST1407 as a highly ASM-resistant strain (MIC, 16 μg/ml) in Japan, suggesting that future epidemiological studies are needed for detecting the spread of this gonococcal antibiotic-resistant phenotype in order to prevent a repetition of the failure that resulted from continuous use of quinolones, producing a high prevalence of quinolone-resistant gonococci.

This study has some limitations. First, the number of tested gonococcal strains may not be enough for definitive conclusions. Second, additional mechanistic investigation may be necessary for further understanding of gonococcal AZM resistance. These limitations should be overcome by our future studies.

In conclusion, a deletion mutation of the *mtrR* promoter region is a possible mechanism of AZM resistance and may be a significant indicator for higher MICs (0.5 μg/ml or higher) in *N. gonorrhoeae* infection. ST4777 was often seen in the lower-MIC group and ST1407, ST6798, and ST6800 in the higher-MIC group, and this correlation with MIC was statistically significant. Further mechanistic studies are needed, including the use of a greater number of strains.

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Surveillance

The second nationwide surveillance of the antimicrobial susceptibility of *Neisseria gonorrhoeae* from male urethritis in Japan, 2012–2013

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ABSTRACT

Worldwide, the most important concern in the treatment of sexually transmitted infections is the increase in antimicrobial resistant *Neisseria gonorrhoeae* strains including resistance to cephalosporins, penicillins, fluoroquinolones or macrolides. To investigate the trends of antimicrobial susceptibility among *N. gonorrhoeae* strains isolated from male patients with urethritis, a Japanese surveillance committee conducted the second nationwide surveillance study. Urethral discharge was collected from male patients with urethritis at 26 medical facilities from March 2012 to January 2013. Of the 151 specimens, 103 *N. gonorrhoeae* strains were tested for susceptibility to 20 antimicrobial agents. None of the strains was resistant to ceftriaxone, but the minimum inhibitory concentration (MIC) 90% of ceftriaxone increased to 0.125 μg/ml, and 11 (10.7%) strains were considered less susceptible with an MIC of 0.125 μg/ml. There were 11 strains resistant to cefixime, and the MICs of these strains were 0.5 μg/ml. The distributions of the MICs of fluoroquinolones, such as ciprofloxacin, levofloxacin and tosufloxacin, were bimodal. Sitafloxacin, a fluoroquinolone, showed strong activity against all strains, including strains resistant to other three fluoroquinolones, such as ciprofloxacin, levofloxacin and tosufloxacin. The azithromycin MICs in 2 strains were 1 μg/ml.

1. Introduction

The antimicrobial resistance of *Neisseria gonorrhoeae* strains against penicillins, tetracyclines, fluoroquinolones, cephalosporins and macrolides is increasing worldwide. Surveillance of the antimicrobial susceptibilities of *N. gonorrhoeae* provides important information for treating gonococcal infections. We have reported the antimicrobial susceptibilities of *N. gonorrhoeae* strains, which were collected at 2009–2010, in the first national surveillance study in Japan [1]. In summary, the rate of less susceptible strains to ceftriaxone was 8.4%; the susceptibility rate to cefixime according to the criteria of the Clinical and Laboratory Standards Institutes (CLSI) [2] was 98.8%; the minimum inhibitory concentrations (MICs) of fluoroquinolones, such as ciprofloxacin, showed a bimodal distribution and resistance rates were 78.3%; sitafloxacn showed low MICs of ≤0.5 μg/ml against ciprofloxacin-resistant strains; the proportion of strains with azithromycin MICs of more than 0.5 μg/ml was 3.6%.

After a ceftriaxone-resistant *N. gonorrhoeae* strain was discovered in a pharyngeal specimen of a female commercial sex worker in Kyoto, Japan [3], other ceftriaxone-resistant *N. gonorrhoeae* strains were discovered in France [4] and Spain [5], but not otherwise in Japan [1,6].

Since 2009, a 2-g azithromycin dose has been accepted by Japanese national insurance for the treatment of both gonococcal and chlamydial urethritis. High-level azithromycin-resistant strains have emerged in many sites worldwide [7–10], and a relationship between the use of azithromycin and an increase in the azithromycin MIC has been described [11]. The Japanese Association of Sexually Transmitted Infections [12] has not recommended the use of azithromycin for treating gonococcal infections. However, some physicians prefer to use azithromycin to treat gonococcal infections, and we anticipate the emergence of high-level azithromycin-resistant strains of *N. gonorrhoeae* in Japan.

In this report, the antimicrobial susceptibility patterns of *N. gonorrhoeae* strains collected from 2012 to 2013 are compared to the patterns from 2009 to 2010 [1]. This national surveillance was conducted by the surveillance committee of three Japanese societies including the Japanese Association of Infectious Diseases, the Japanese Society of Chemotherapy and the Japanese Society of Clinical Microbiology. The committee has previously performed and published other surveillance studies regarding the antimicrobial susceptibilities of pathogens causing respiratory infections, urinary tract infections, urethritis and surgical site infections. The present surveillance study was the second study performed on *N. gonorrhoeae* strains collected from male patients with gonococcal urethritis.

2. Materials and methods

2.1. Patients and participating facilities

The targets were male patients older than 16 years with urethral discharge and symptoms of urethritis, such as pain upon micturition, urethral pain or urethral discomfort. Included patients were diagnosed with gonococcal urethritis by a clinician. The period of specimen collection was between March 2012 and January 2013. The 38 participating facilities included departments of urology in hospitals and private clinics that specialized in urology or urology and dermatology in Japan. The clinicians who participated in this study explained the purpose of the study to the patients orally or through written documents and obtained the written consent of each patient. This study was approved by the ethical committee of each facility. The facilities that did not have an ethical committee submitted this study to the ethical committee of the specific non-profit organization CREC net, Kitakyushu, Japan, which approved it.

2.2. Specimens and patient information

The discharge from the urethral meatus was collected with a sterilized cotton swab, placed in transport agar (SEEDSWAB γNo2, Eiken Chemical Co. Ltd., Tokyo, Japan) and sent at room temperature to the Infection Scientific Control Research Center, The Kitasato Institution, Tokyo, Japan. Only one specimen was collected from each patient. The patient's information, including age, diagnosis and the properties of the discharge were reported for each sample.

2.3. Isolation of N. gonorrhoeae strains and antimicrobial susceptibility testing

The bacterial isolation and antimicrobial susceptibility testing were performed in the Infection Scientific Control Research Center, The Kitasato Institution, Tokyo, Japan. For each specimen, *N. gonorrhoeae* strain isolation and identification was attempted.

The antimicrobial susceptibility testing was performed according to the CLSI Document M100-S22 [2], and the minimum inhibitory concentrations (MICs) were determined by the agar dilution method. Supplemented 1% GC agar (1.1 g L-cysteine, 0.03 g guanine HCL, 3 mg thiamine HCL, 13 mg para-aminobenzoic acid, 0.01 g B12, 0.1 g cocarboxylase, 0.25 g nicotinamide adenine dinucleotide, 1 g adenine, 10 g L-glutamine, 100 g glucose, and 0.02 g ferric nitrate per liter) was used for determining the MICs. When the MIC of carbapenems or clavulanic acid was measured, cysteine was not included in the agar. The range of concentrations for testing included 12 two-fold serial dilutions (128–0.063 μg/ml) of antimicrobials, but the starting concentration fluctuated depending on the particular type of antimicrobial used. The inoculum was adjusted to a 0.5 MacFarland standard by the direct adjustment method. The *N. gonorrhoeae* strains were cultured at 36 ± 1 °C in 5% CO_2 atmosphere overnight. *N. gonorrhoeae* ATCC 49226 was used as the standard control.

The MICs of the following 20 antimicrobial agents were measured: penicillin G, ampicillin, amoxicillin, clavulanic acid-amoxicillin, cefpodoxime, cefdinir, cefixime, cefditoren, ceftriaxone, cefodizime, flomoxef, aztreonam, meropenem, spectinomycin, ciprofloxacin, levofloxacin, tosufloxacin, sitafloxacin, minocycline and azithromycin. The susceptibility or resistance of the isolate to each antibiotic was determined according to CLSI Document M100-S22 [2].The antimicrobial susceptibility data in this surveillance were compared with those in the first surveillance.

β-lactamase activity in the *N. gonorrhoeae* isolates was detected by the nitrocefin method (Cefinase Disk™; BD BBL™). The *N. gonorrhoeae* strains that were resistant to penicillin G (MIC: ≥2 μg/ml) and in which β-lactamase activity was detected were determined to be penicillinase-producing *N. gonorrhoeae* (PPNG). Among β-lactamase-non-producing strains, strains that were resistant to penicillin G (MIC: ≥2 μg/ml) were determined to be chromosomally mediated resistant *N. gonorrhoeae* (CMRNG).

The threshold MICs for antimicrobial resistance are assumed according to the following criteria: ≥2 μg/ml of penicillin G, ≥2 μg/ml of minocycline, ≥1 μg/ml of cefpodoxime, ≥1 μg/ml of ciprofloxacin or ≥0.5 μg/ml of azithromycin. The phenotypes of *N. gonorrhoeae* strains were classified by their resistance to antimicrobial agents.

3. Results

3.1. Number of specimens and isolated strains

Of the 152 specimens from 26 medical facilities, one was omitted because the patient's age was 14 years. The median age was 32 years (range: 18–65), and 39.7% and 33.8% of specimens were collected from patients in their 20s and 30s, respectively. The urethral discharge was described as purulent for 139 specimens and serous for 11. Of the 151 specimens from 151 patients, 103 strains could be cultured and identified as *N. gonorrhoeae*. From the 139 purulent specimens, 100 strains (71.9%) were isolated. Of these 103 strains, 36, 21, 16, 14, 9 and 7 strains were collected from the Kyushu, Chugoku, Kinki, Chubu, Tohoku and Tokyo areas, respectively.

3.2. Antimicrobial susceptibilities

Antimicrobial susceptibility testing was performed on all 103 isolated strains (Table 1). None was susceptible to penicillin G (MIC: ≤0.06). Only two strains (1.9%) were determined to be PPNG, and the MICs of penicillin G to these strains were 2 and 32 μg/ml. The MIC of clavulanic acid-amoxicillin MIC to PPNG strains was 0.5 μg/ml. Among β-lactamase-non-producing strains, 21 strains (20.8%) had higher MICs to penicillin G (MIC ≥2 μg/ml, range: 2–4 μg/ml) and were determined to be CMRNG. The MIC_{90} of four kinds of penicillins including penicillin G, ampicillin, amoxicillin and amoxicillin-clavulanic acid for β-lactamase-non-producing strains was 2 μg/ml.

The MICs of minocycline for two PPNG strains were also higher (8 and 16 μg/ml). The MIC range for minocycline in the β-lactamase-non-producing strains was ≤0.06–32 μg/ml and 3 strains (2.9%) were resistant to minocycline. (MIC: 16 or 32 μg/ml).

The susceptibility rates of all the strains to oral cephalosporins such as cefixime and cefpodoxime were 89.3% and 59.2% according to CLSI criteria [2], respectively. The susceptibility of cefixime evidently decreased compared to the strains collected in the first surveillance study. The MICs of the parenteral cephalosporins ceftriaxone and cefodizime were relatively low. The high-level ceftriaxone-resistant strains, such as Ohnishi's report [3], were not found in the surveillance. The MIC_{90} of ceftriaxone increased from ≤0.06 μg/ml in the first surveillance study to 0.125 μg/ml in this study. All 11 strains with a ceftriaxone MIC of 0.125 μg/ml had cefixime MICs of 0.25 or 0.5 μg/ml. However, 3 strains with cexifime MIC of 0.5 μg/ml had a ceftriaxone MIC of ≤0.06 μg/ml.

The MIC distribution for fluoroquinolones, such as ciprofloxacin, levofloxacin and tosufloxacin, showed bimodal. The MICs of these three antimicrobials for the 21 susceptible strains were ≤0.06 μg/ml. The MIC of sitafloxacin was lower than that of the other fluoroquinolones. Strains with ciprofloxacin MICs of ≤0.06 μg/ml had also sitafloxacin MIC of ≤0.06 μg/ml. Strains with ciprofloxacin MICs between 0.5 and 32 μg/ml showed sitafloxacin MIC of ≤0.06, 0.125 or 0.25 μg/ml. Only one strains with sitafloxacin MIC of 0.5 μg/ml and ciprofloxacin MIC of 64 μg/ml was newly identified.

Strains with resistance to spectinomycin were not identified in this study. No high-level azithromycin resistant strains were found, but two strains had an MIC of 1 μg/ml.

3.3. Phenotypes of antimicrobial resistance among N. gonorrhoeae strains

Table 2 shows the antimicrobial resistance phenotypes of the strains. Among the isolated strains, 83 (80.6%) met resistance criteria to one or more tested antimicrobials and 34 were resistant to a single antimicrobial (ciprofloxacin: 33 azithromycin 1). Forty-nine strains (47.5%) showed resistance to more than two types of antimicrobials such as penicillins, cephalosporins, tetracyclines, fluoroquinolones and macrolides.

Table 1
Antimicrobial MIC distribution for 103 *N. gonorrhoeae* strains.

Antibacterial agent	MIC (μg/ml)														
	≤0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥256	MIC_{50}	MIC_{90}
Penicillin G		6	24	17	33	20	2			1				1	2
Ampicillin		8	14	11	29	33	7				1			1	2
Amoxicillin			21	8	20	52	1				1			2	2
Clavulanic acid-amoxicillin		1	21	10	25	46								1	2
Cefpodoxime	38	3	5	15	23	17	2							0.5	2
Cefdinir	41		2	25	35									0.5	1
Cefixime	42	8	42	11										0.25	0.5
Cefditoren	52	24	22	5										≤0.06	0.25
Ceftriaxone	92	11												≤0.06	0.125
Cefodizime	79	21	3											≤0.06	0.125
Flomoxef		3	20	8	22	41	9							1	2
Aztreonam	10	15	14	2	1	1	38	22						4	8
Meropenem	68	35												≤0.06	0.125
Spectinomycin								3	95	5				16	16
Ciprofloxacin	21			1		1	13	18	36	12	1			8	32
Levofloxacin	21			1	1	6	26	38	10					4	8
Tosufloxacin	21			3	4	31	14	19	11					2	16
Sitafloxacin	38	32	32	1										0.125	0.25
Minocycline	2	29	26	40	1			1	3	1				0.25	0.5
Azithromycin	15	44	39	3	2									0.125	0.25

4. Discussion

The guideline of the Japanese Association of Sexually Transmitted Infections recommends that gonococcal urethritis and cervicitis be treated with 1 g of ceftriaxone in a single intravenous dose, 1 g of cefodizime in a single intravenous dose and 2 g of spectinomycin in a single intramuscular dose [12]. This recommendation did not change during the first and second surveillance studies. The second surveillance study revealed that the patient demographics and clinical features of the urethral discharges were the same as in the first study, although the antimicrobial susceptibility data were different.

The prevalence of PPNG decreased compared to the first surveillance data. Previous to 2009, the prevalence of PPNG in Japan had been approximately 1% [13]. However, the prevalence was 7.2% in the first surveillance study. The second surveillance data showed the prevalence of PPNG to be 0.2%, which is a return to historic levels. We are not able to explain why the prevalence was higher in 2009–2010. One explanation is that patients who were infected in foreign countries were included in the first study. Penicillins are not available for the treatment of gonococcal infections in Japan. No strain was sensitive to penicillin G in this study. In addition, penicillin with a β-lactamase inhibitor cannot be recommended to treat gonococcal urethritis, because the MICs of amoxicillin are relatively higher and the MIC of clavulanic acid-amoxicillin was not low for PPNG strains (0.5 μg/ml).

Table 2
The phenotypes of antimicrobial resistance among *N. gonorrhoeae* strains.

Antimicrobials					Numbers
Penicillin G	Minocycline	Cefpodoxime	Ciprofloxacin	Azithromycin	
			R		33
				R	1
R	R				1
R			R		1
		R	R		22
	R		R		3
			R	R	1
R		R	R		17
R	R		R		1
R		R	R	R	3

R: Resistance to antimicrobial agents that was determined by the criteria below. MICs of ≥2 μg/ml of penicillin G, ≥2 μg/ml of minocycline, ≥1 μg/ml of cefpodoxime, ≥1 μg/ml of ciprofloxacin or ≥0.5 μg/ml of azithromycin.

The most serious problem for the treatment of gonococcal infections worldwide is the increase in cephalosporin-resistant strains. We did not find further evidence of high-level ceftriaxone-resistant strains in Japan. However, ceftriaxone-resistant strains were reported from France and Spain [4,5] and there are reports of ceftriaxone treatment failure in patients with *N. gonorrhoeae* strains isolated from the pharynx [14–17]. In particular, Swedish case-report described a *N. gonorrhoeae* strain with a ceftriaxone MIC of 0.25 μg/ml that was detected from the pharynx of a male patient after treatment with 250 mg and 500 mg of ceftriaxone; this patient was most likely infected through unprotected oral sex with a female partner in Japan [14]. This indicates that some women in Japan have *N. gonorrhoeae* strains with a high ceftriaxone MIC, but these strains were not found in any surveillance. Indeed, the MIC_{90} of ceftriaxone increased from ≤0.06 μg/ml in the first surveillance study to 0.125 μg/ml in this study. The strains with a ceftriaxone MIC of 0.125 μg/ml, those are termed as "less susceptible strains," increased. In addition, the strains sensitive to cefixime with an MIC ≤0.06 μg/ml, which Deguchi recommended as the breakpoint MIC of cefixime in Japan [18], decreased from 55.4% to 40.8%. These resistance or those less susceptibility in *N. gonorrhoeae* to cephalosporins are closely related to the mosaic structure of *penA* gene which codes for PBP2 [4,5,19,20]. Our data are evidence that this type of resistance has been spreading in Japan.

The MICs of fluoroquinolones did not differ between the first and second surveillance studies. The fluoroquinolone-resistant rates of strains have shown nearly the same level as in Tanaka's reports [21]. This likely means that physicians treating gonococcal infections are complying with the guidelines of the Japanese Society of Sexually Transmitted Infections. The activity of sitafloxacin remains stable in two our surveillances. As described previously [1], sitafloxacin has activity against ciprofloxacin-resistant *N. gonorrhoeae* strains. Sitafloxacin can be one of treatment options for untreatable *N. gonorrhoeae* strains. However, one strains with sitafloxacin MIC of 0.5 μg/ml was found and further observation or clinical study would be necessary.

In both the first and second surveillance study, high-level resistant strains to azithromycin were not found. The main mechanism for azithromycin-resistance in *N. gonorrhoeae* is mutations of the macrolide target, 23S rRNA as A2059G or C2611T mutations [7–10,20]. *N. gonorrhoeae* has four 23S rRNA alleles and the resistance to azithromycin depends on the numbers of alleles with mutations [20]. Unemo described that the azithromycin MIC increase to 4,096 μg/ml in strains with A2059G mutations in three or four alleles, but the MICs of strains with the mutation in one allele are not changed as wild-type strains [10]. Through this theory, at least two strains (1.9%) with an azithromycin MIC of 1 μg/ml have mutations in more than 2 alleles of the 23S rRNA. In other Japanese surveillance data, 3.6% (7/193) of strains in the Kyoto and Osaka areas or 6.6% (8/122) of strains in the Tokyo area were resistant to azithromycin (>0.5 μg/ml) [6,22]. In the Tokyo area, higher-resistant strains were found (one and two strains with MIC 16 and 8 μg/ml, respectively). Yasuda et al. showed clinical study using azithromycin 2g in Japan and strains with MIC 2 or 4 μg/ml of azithromycin remained after the treatment [23]. Among strains with MIC 1 or 0.5 μg/ml eradication rates were 58% (7/12) and 97% (31/32), respectively. Even if azithromycin 2g is used, a high dose of azithromycin could covered only strains with MIC ≤0.5 μg/ml and we wonder that azithromycin-resistance would increase.

Table 2 shows the numbers of strains according to the antimicrobial resistant phenotype. Among 103 strains, 20 were classified as "not resistant" to all antimicrobials. These strains were 20 of 21 the strains with ciprofloxacin MIC ≤0.06 μg/ml (another one had an azithromycin MIC of 0.5 μg/ml). Regarding *N. gonorrhoeae* strains in Japan, the susceptibility for fluoroquinolone, which are less frequently used now is important. According to Tapsall's criteria for multi-drug resistant *N. gonorrhoeae* (MDR-NG) [24], 42 strains (40.1%) met the criteria of MDR-NG. In 2009–2010, 39.8% of the strains were classified as MDR-NG, which was quite similar to the proportion in 2011–2012.

The next Japanese antimicrobial surveillance initiative for *N. gonorrhoeae* is planned for 2016. The increase in cephalosporin-resistance is more prominent worldwide. Dual therapies, such as ceftriaxone plus azithromycin or ceftriaxone and effective quinolones are recommended and being used worldwide. The recommendation of Japanese Association of Sexually Transmitted Infections for treating gonococcal infections has remained the same. The purpose of the next surveillance study is to evaluate the appropriateness of the present recommendation for the treatment of gonococcal infection and to determine whether the recommendation should be modified.

Conflicts of interest

Mitsuru Yasuda has received donation from Astellas Pharma Inc. Akira Watanabe has received speaker's honorarium from MSD K.K., Glaxo SmithKline K.K., Shionogi & Co., Ltd., Daiichi Sankyo Co., Ltd., Taisho Toyama Pharmaceutical Co., Ltd. and Pfizer Japan Inc.; grant support from Kyorin Pharmaceutical Co., Ltd., Shionogi & Co., Ltd.

Taisho Pharmaceutical Co., Ltd., Toyama Chemical Co., Ltd., Daiichi Sankyo Co., Ltd., Sumitomo Dainippon Pharma Co., Ltd., Taiho Pharmaceutical Co., Ltd. and Meiji Seika Pharma Co., Ltd. Satoshi Iwata has received speaker's honorarium from Astellas Pharma Inc., Pfizer Japan Inc., Taisho Toyama Pharmaceutical Co., Ltd., MSD K.K., Meiji Seika Pharma Co., Ltd., Daiichi Sankyo Co., Ltd. and Japan Vaccine Co., Ltd., donation from Taisho Toyama Pharmaceutical Co., Ltd. and supported, in part, by a fund from Nikon Corporation. Mitsuo Kaku has received speaker's honorarium from Taisho Toyama Pharmaceutical Co., Ltd., Shionogi & Co., Ltd., Pfizer Japan Inc. and Sumitomo Dainippon Pharma Co., Ltd. and donation from Astellas Pharma Inc. Junichi Kadota has received speaker's honorarium from Taisho Toyama Pharmaceutical Co., Ltd., Pfizer Japan Inc., MSD K.K., Kyorin Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Glaxo SmithKline K.K., payments for a manuscript drafting and editing from Nankodo Co., Ltd. and donation from Astellas Pharma Inc. Keisuke Sunakawa has received speaker's honorarium from Taisho Toyama Pharmaceutical Co., Ltd., Toyama Chemical Co., Ltd. and Meiji Seika Pharma Co., Ltd. Hideaki Hanaki is a member of a laboratory endowed chair from Kohjin Bio Co., Ltd. Taiji Tsukamoto has received speaker's honorarium from Astellas Pharma Inc., and payments for a manuscript drafting and editing from RichHill Medical Inc. Shin Egawa has received donation from Takeda Pharmaceutical Co., Ltd., Astellas Pharma Inc., Asahi Kasei Corp. and Euro Meditech Co., Ltd. Soichi Arakawa has received speaker's honorarium from Taisho Toyama Pharmaceutical Co., Ltd.

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平成25年7モデル県の性感染症診察医療機関全数調査推計有病率と国立感染症研究所の定点報告推計有病率の比較～7県医療機関全数調査結果と定点調査報告結果の有病率はなぜ乖離したのか?

Clarification of differences between the prevalence rate of sexually transmitted infections from a sentinel survey of medical institutions in seven model prefectures and that estimated by fixed point observation of all 47 prefectures by the Japanese Government : Why does the Japanese Government's data deviate from the sentinel survey data?

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本研究の目的は全国7モデル県の性感染症の医療機関全数調査結果の有病率と国立感染症研究所の定点報告数から定点有病率を推計し、性感染症定点調査報告にどのような問題があるかを検証することである。

本研究は、岩手県、茨城県、千葉県、富山県、岐阜県、兵庫県、徳島県の7県を調査モデル県とし、産婦人科、泌尿器科、皮膚科、性病科を標榜する平成25年の医療機関を対象とした。調査期間は平成25年10月とし、医師が受診日・性・年齢・診断した性感染症を調査票に記録した。県調査担当者が調査票を回収した。調査票を電算化し、7県全調査推計有病率と性感染症定点推計有病率と比較した。

回収率は67.3%であった。男性淋菌感染症及び女性性器クラミジア症について7県全数調査推計有病率（47都道府県を推計）と定点推計有病率は乖離があり前者が多かった。これは保健所の定点選択に問題が有り、本研究と定点調査報告推計有病率に乖離が起きたと考えられる。

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Although a remarkable prevalence of sexually transmitted infections (STIs) exists in Japan, precise epidemiological data of STIs from all OB/GYN, urology, and venereology physicians is lacking. We conducted a sentinel survey of STIs diagnosed in 7 model prefectures in Japan from 2012 to 2014.

We sent a questionnaire to all of the above physicians in 7 model prefectures in early October 2013. We asked them to answer the questions about patients' demographics and diagnosis of various STIs made in October 2013. The response rate was 67.3%. We calculated our prevalence rate (person-years) per 100,000 people infected with STIs from the 7 model prefectures and compared it to Japanese Government's fixed-points observation rate from all 47 prefectures. The survey data from the 7 prefectures showed that the rate of male genital gonococcal infection was about 2.7 times higher and that of female genital chlamydial infection, especially in women aged 20 to 24 years, was 6.1 times higher than that shown by the Government.

The STIs showed a decreasing trend at fixed points from 2002 to 2009 and sudden levelling off in the Government's data. Although comparison of our actual data with the Government's data is difficult, discrepancies were found between the Government's data showing a decreasing trend in STIs and our data, which indicated that STIs did not decrease in these periods. Further, rates by gender and individual STI cannot be compared with fixed-point data. Our sentinel survey data appears to be better balanced than that of the fixed-point data.

Key words : sentinel surveillance, fixed point observation, national data, male gonococcal urethritis, chlamydial cervicitis

緒 言

感染症の予防及び感染症の患者に対する医療に関する法律（以降、法）第十四条において、都道府県知事は感染症の発生の状況及び動向の把握を行わなければならない。また同法感染症の予防及び感染症の患者に対する医療に関する法律施行規則（以降、規則）第六条によって指定される感染症は法第十四条第一項に規定する厚生労働省令で定める五類感染症のうち、発生の状況の届出を担当させる指定届出機関の指定した地域における感染症に係る医療を提供する体制、保健所の設置の状況、人口等の社会的条件、地理的条件等の自然的条件その他の地域の実情を勘案して、病院又は診療所のうち当該五類感染症指定区分の感染症に係る指定届出機関として適当と認めるものについて行うものと規定されている。

また性感染症は規則第二条に性器クラミジア感染症、性器ヘルペスウイルス感染症、尖圭コンジローマ及び淋菌感染症が特定感染症予防指針の対象性感染症として、国は法第十一条に基づいて作成する義務があり、性感染症に関する特定感染症予防指針が公表された[1]。この指針で性感染症罹患率を下げるため、基礎情報として性感染症定点動向調査の活用のみならず、国は性感染症の発生動向に関する各種疫学研究を強化し、性感染症の全数調査についての研究を行うべきことも述べている。

諸外国でも同様の感染症サーベイランスが実施されている[2-4]が、トレンド把握を目的としているのがほとんどである。わが国の感染症定点調査報告の理論的背景と特徴は、保健所が無作為に医療機関を選択し、そこからの患者報告を保健所が集計し、国立感染症研究所に集計結果を送付する。同研究所が感染症動向調査としてトレンド把握を目的とし[5]、感染症ごとの全国罹患数推計のための定点設計をしている[6]。小児定点、インフルエンザ定点からの罹患数推計数は公表されているが、性感染症定点の推計数は算出されておらず、定点設計の根本である定点設定を保健所が無作為に行っていないと考えられるため、疫学計算・公表が難しいと考える[7]。

本研究の目的は、性感染症に関する特定感染症予防指針の「定点調査の補強」に則り、国立感染症研究所性感染症定点動向調査報告（以降、性感染症定点調査報告）有病率の確からしさが本研究の全国７モデル県の性感染症の医療機関全数調査（以降、７県全数調査）結果の有病率を上回っているか、また性感染症定点調査報告にどのような問題があるかを検証することである。

対象と方法

本研究は、岩手県、茨城県、千葉県、富山県、岐阜県、兵庫県、徳島県の７県を調査モデル県とし、対象科は、産婦人科（産科のみ、婦人科のみを含む）、泌尿器科（皮膚泌尿器科を含む）、皮膚科、性病科を標榜する平成 25