Table 2 Comparison of susceptibility (MIC_{50} and MIC_{90}) in 11 kinds of antimicrobial agents against *N. gonorrhoeae*

	MIC_{50}/MIC_{90} of antimicrobials				
Antimicrobials	Range	MIC_{50}	MIC_{90}	Sensitive rates (%)	Resistant rates(%)
PCG	0.016-16	1	4	6.7	93.3
MINO	0.06-32	0.25	0.5	55.8	44.2
CTRX	0.004-0.25	0.032	0.12	100	0
CFIX	0.004-0.25	0.016	0.25	90	10
CDZM	0.004-0.26	0.016	0.06	100	0
SPCM	1-32	16	16	100	0
AZM	0.03-4	0.064	0.25	98.3	1.7
LVFX	0.016-8	4	8	24.2	75.8
STFX	0.016-0.5	0.06	0.25	100	0
PIPC	0.004-0.25	0.25	0.25	100	0
MEPM	0.004-0.125	0.03	0.06	100	0

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J Infect Chemother (2013) 19:571–578
DOI 10.1007/s10156-013-0637-2

SURVEILLANCE

Nationwide surveillance of the antimicrobial susceptibility of *Neisseria gonorrhoeae* from male urethritis in Japan

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Received: 24 March 2013 / Accepted: 11 June 2013 / Published online: 28 June 2013

Abstract *Neisseria gonorrhoeae* is one of the most important pathogens causing sexually transmitted infection, and strains that are resistant to several antimicrobials are increasing. To investigate the trends of antimicrobial susceptibility among *N. gonorrhoeae* strains isolated from male patients with urethritis, a Japanese surveillance committee conducted the first nationwide surveillance. The urethral discharge was collected from male patients with urethritis at 51 medical facilities from April 2009 to October 2010. Of the 156 specimens, 83 *N. gonorrhoeae* strains were tested for susceptibility to 18 antimicrobial agents. The prevalence of β-lactamase-producing strains and chromosomally mediated resistant strains were 7.2 % and 16.5 %, respectively. None of the strains was resistant to ceftriaxone, but the minimum inhibitory concentration (MIC) of ceftriaxone for 7 strains (8.4 %) was

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0.125 μg/ml. One strain was resistant to cefixime (MIC 0.5 μg/ml). The MICs of fluoroquinolones, such as ciprofloxacin, levofloxacin, and tosufloxacin, showed a bimodal distribution. The MIC of sitafloxacin was lower than those of the three fluoroquinolones listed here, and it was found that the antimicrobial activity of sitafloxacin was stronger than that of the fluoroquinolones. The MIC of azithromycin in 2 strains was 2 μg/ml, but no high-level resistance to macrolides was detected.

Keywords Neisseria gonorrhoeae · Nationwide surveillance · Antimicrobial susceptibilities · Japan

Introduction

Neisseria gonorrhoeae is one of the most important pathogens that cause male urethritis and female cervicitis as a sexually transmitted infection (STI). *N. gonorrhoeae* is vulnerable to high temperatures, low temperatures, and drying, so that its survival is difficult in the general environment. *N. gonorrhoeae* transmits from human to human as an STI to maintain the species. When antimicrobials are used for humans, *N. gonorrhoeae* has been also exposed to many antimicrobials in vivo and may continue to survive despite antimicrobial pressure by acquiring drug-resistant mechanisms.

When penicillin was developed, penicillin showed powerful antimicrobial activity against *N. gonorrhoeae* and was extremely clinically effective against gonococcal infections. However, some populations of *N. gonorrhoeae* strains produced penicillinase, and penicillinase-producing *N. gonorrhoeae* (PPNG) spread throughout the world. In Japan, it has been recently estimated that the prevalence of PPNG was less than 1 % [1, 2], although, historically, it has reached approximately 16 % [3]. Moreover, chromosomally mediated resistance to β-lactams has emerged and is spreading. The first *N. gonorrhoeae* strain with resistance to the oral third-generation cephalosporins in Japan was reported in 2001 [4]. The resistance of *N. gonorrhoeae* strains to cefixime, which is one of the antimicrobial agents recommended for the treatment of gonococcal infections by the American CDC [5] and many other countries, has also been reported [6, 7]. In addition, a ceftriaxone-resistant *N. gonorrhoeae* strain was isolated from the pharynx of a female sex worker in Japan [8]. The prevalence of fluoroquinolone resistance among *N. gonorrhoeae* strains has reached almost 70 % [9, 10]. In many countries, azithromycin-resistant *N. gonorrhoeae* strains have also emerged [11].

Given the situation just described, attention to the antimicrobial susceptibility of *N. gonorrhoeae* has risen, and surveillance of the antimicrobial susceptibility of *N. gonorrhoeae* has been performed by individual laboratories in some areas of Japan [12–14]. The surveillance committee in three Japanese societies, including the Japanese Association of Infectious Diseases, the Japanese Society of Chemotherapy, and the Japanese Society of Clinical Microbiology, has previously performed and published

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other surveillances regarding antimicrobial susceptibilities of pathogens of respiratory infections [15] and urinary tract infections [16]. The surveillance committee of these three societies has now conducted the first nationwide survey of the antimicrobial susceptibility of *N. gonorrhoeae*.

Materials and methods

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. The patients were diagnosed with gonococcal urethritis by a clinician. The period of specimen collection was between April 2009 and October 2010. The 51 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.

Specimens and patient information

Discharge from the urethral meatus was collected with a sterilized cotton swab, placed in transport agar (BD BBL Cultureswab EZII; Becton-Dickinson, Tokyo, Japan) and sent to the Infection Scientific Control Research Center, The Kitazato Institution, Tokyo, Japan, at room temperature. Only one specimen was collected from each patient. The patient's information, including age and diagnosed diseases, and the properties of the discharge were reported for each sample.

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

Bacterial isolation and antimicrobial susceptibility testing were performed in the Infection Scientific Control Research Center, The Kitazato Institution, Tokyo, Japan. For each specimen, *N. gonorrhoeae* strain isolation and identification were attempted. In addition, genetic identification was performed using a nucleic acid amplification test (Cobas amplicore STI-1; Rosche Diagnostic Japan, Tokyo, Japan).

The antimicrobial susceptibility testing was performed according to the Clinical and Laboratory Standards Institute (CLSI) Document M7-A8 (M100-S21) [17], 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 B_{12}, 0.1 g cocarboxylase, 0.25 g NAD, 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 clavulanic acid was measured, cysteine was not included in the agar. The range of concentrations for testing included 12 twofold serial dilutions (128–0.063 μg/ml of

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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 a 5 % CO_2 atmosphere for 20–24 h. *N. gonorrhoeae* ATCC 49226 was used as the standard control.

The MICs of the following 18 antimicrobial agents were measured: ampicillin, amoxicillin-clavulanic acid, penicillin G, cefixime, cefditoren, cefpodoxime, cefdinir, ceftriaxone, cefodizime, flomoxef, aztreonam, spectinomycin, ciprofloxacin, levofloxacin, tosufloxacin, sitafloxacin, minocycline, and azithromycin. The susceptibility or resistance of the isolate to each antibiotic was determined according to CLSI Document M7-A8 [17].

β-Lactamase activity in the isolated *N. gonorrhoeae* was detected by the nitrocefin method (Cefinase Disk; Becton–Dickinson). The *N. gonorrhoeae* strains that were resistant to penicillin G (MIC ≥2 μg/ml) and in which β-lactamase activity was detected were determined as PPNG. Among β-lactamase non-producing strains, strains that were resistant to penicillin G (MIC ≥2 μg/ml) were determined as chromosomally mediated resistant *N. gonorrhoeae* (CMRNG).

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

Results

Number of specimens and isolated strains

Of the 156 specimens from 156 patients, 144 were positive for *N. gonorrhoeae* by polymerase chain reaction (PCR), but only 84 strains could be isolated by culture and identified as *N. gonorrhoeae*. Of these 84 strains, 31, 20, 12, 10, 5, 5, and 1 strain(s) were collected from the Kyushu, Chubu, Kinki, Tohoku, Tokyo, Chugoku, and Hokkaido areas, respectively.

The median age of the patients was 29 years (range, 16–66 years old). The urethral discharge was described as purulent for 149 samples and serous for 5 samples. The positive rates for *N. gonorrhoeae* by PCR were 93.3 % in the purulent samples and 100 % in the serous samples. The success rates for culture were 54.3 % and 20 % for the purulent and serous samples, respectively.

Antimicrobial susceptibilities

Among the 84 isolated strains, 83 strains were available for antimicrobial susceptibility testing (Table 1). Of these strains, only one strain was susceptible to penicillin G (MIC ≤0.06), and the susceptibility rate of all the strains to penicillin G was 1.2 %. Six strains (7.2 %) were determined as PPNG because of identification of β-lactamase, and the MIC of penicillin G for these strains was ≥2 μg/ml (range, 2–64 μg/ml). The MIC_{90}s of penicillin G, ampicillin, and

Table 1 Antimicrobial MIC distribution for 83 *Neisseria gonorrhoeae* strains

Antibacterial agent	Minimum inhibitory concentrations (MICs) (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	1	12	9	8	25	19	4	3	1		1			1	4
Ampicillin		12	8	6	24	24	3	1	3	1		1		1	4
Amoxicillin -clavulanic acid			19	7	31	26								1	2
Cefpodoxime	34	5	5	7	21	10	1							0.25	2
Cefdinir	42	1	4	28	8									≤0.06	0.5
Cefixime	46	13	23	1										≤0.06	0.25
Cefditoren	29	22	25	7										0.125	0.25
Ceftriaxone	76	7												≤0.06	≤0.06
Cefodizime	52	24	7											≤0.06	0.125
Flomoxef		5	14	11	9	38	6							2	2
Aztreonam	3	17	11	10	3	4	23	12						1	8
Spectinomycin							9	65	9					8	16
Ciprofloxacin	18					3	10	19	27	6				8	16
Levofloxacin	18					10	24	30	1					4	8
Tosufloxacin	18				1	9	38	7	10					4	16
Sitafloxacin	30	16	37											0.125	0.25
Minocycline	5	14	16	36	7		1	1	3					0.5	1
Azithromycin	10	44	26	1		2								0.125	0.25

amoxicillin-clavulanic acid in PPNG strains were 64, 128, and 2 μg/ml, respectively. Among β-lactamase non-producing strains, 22 strains (26.5 %) had higher MICs to penicillin G (MIC ≥2 μg/ml; range, 2–4 μg/ml) and determined as CMRNG. The MIC_{90}s of penicillin G, ampicillin, and amoxicillin-clavulanic acid in the β-lactamase non-producing strains were all 2 μg/ml.

The MIC range for minocycline in the β-lactamase-producing strains was 0.25–16 μg/ml. One strain was susceptible to minocycline. In contrast, the MIC range for minocycline in the β-lactamase non-producing strains was ≤0.06–16 μg/ml, and only one strain was resistant to minocycline (MIC 16 μg/ml).

The rates of susceptibility of all the strains to oral cephalosporins, including cefixime and cefpodoxime, were 98.8 % and 61.4 %, respectively. Only one strain had a MIC of 0.5 μg/ml for cefixime, and the MIC of this strain was not included in the susceptible category according to the CLSI document. Regarding the parenteral cephalosporins, the MICs of ceftriaxone and cefodizime were relatively low; the MIC_{90}s for all the strains were ≤0.06 and 0.125 μg/ml, respectively. None of the strains was resistant to ceftriaxone according to the CLSI document, but seven strains (8.4 %) had a MIC of 0.125 μg/ml for this antimicrobial.

The MIC distribution for fluoroquinolones, such as ciprofloxacin, levofloxacin, and tosufloxacin, was bimodal. The MICs of these antimicrobials for the 16 susceptible strains were ≤0.06 μg/ml, and these strains were all β-lactamase non-producing strains. The MIC of sitafloxacin was lower than that of the other fluoroquinolones. Among the 30 strains that had a MIC ≤ 0.06 μg/ml for sitafloxacin, 12 of the strains were resistant to other fluoroquinolones. All the strains that had MICs of 0.125 or 0.25 μg/ml for sitafloxacin were also resistant to other fluoroquinolones (Table 2).

Table 2 Relationship between MICs of sitafloxacin, ciprofloxacin, levofloxacin, and tosufloxacin

N. gonorrhoeae strains	MIC_{50} and MIC_{90} to three fluoroquinolones (μg/ml)		
	Ciprofloxacin	Levofloxacin	Tosufloxacin
Strains with MIC ≤0.06 μg/ml sitafloxacin (n = 30)			
MIC_{50}	≤0.06	≤0.06	≤0.06
MIC_{90}	4	4	4
Strains with MIC 0.125 μg/ml sitafloxacin (n = 16)			
MIC_{50}	8	4	8
MIC_{90}	32	8	16
Strains with MIC 0.25 μg/ml sitafloxacin (n = 37)			
MIC_{50}	16	4	4
MIC_{90}	32	8	16

Table 3 Antimicrobial resistance patterns among *N. gonorrhoeae* strains

Combinations of resistance to antimicrobial agents	*n*
Ciprofloxacin	22
Ciprofloxacin + penicillin G	6
Ciprofloxacin + penicillin G + minocycline	3
Ciprofloxacin + penicillin G + minocycline + cefpodoxime	1
Ciprofloxacin + penicillin G + cefpodoxime	14
Ciprofloxacin + penicillin G + cefpodoxime + cefixime	1
Ciprofloxacin + penicillin G + azithromycin	2
Ciprofloxacin + cefpodoxime	15
Ciprofloxacin + azithromycin	1
Total	65

Resistance to antimicrobial agents was determined by the following criteria: MICs ≥2 μg/ml penicillin G, ≥2 μg/ml minocycline, ≥1 μg/ml cefpodoxime, ≥0.5 μg/ml cefixime, ≥1 μg/ml ciprofloxacin, or ≥0.5 μg/ml azithromycin

Strains with resistance to spectinomycin were not found in this study. Regarding azithromycin, 2 strains had a MIC of 2 μg/ml, but no high-level resistant strains were found.

Antimicrobial resistance patterns among *N. gonorrhoeae* strains

N. gonorrhoeae strains could be classified by the combinations of resistance to antimicrobial agents, and 65 *N. gonorrhoeae* strains met the resistance criteria for some antimicrobials (Table 3): all the 65 strains were resistant to ciprofloxacin, 49 of the strains were resistant to penicillin G, and 31 of the strains were resistant to cefpodoxime. Eighteen of the strains did not meet any resistant criteria, but only 1 strain was susceptible to all the antimicrobial agents tested.

Discussion

The antimicrobial resistance of *N. gonorrhoeae* is increasing worldwide. In particular, β-lactam- and fluoroquinolone-resistant strains are known to be spreading in the Western Pacific region. The treatment of gonococcal infections is difficult in Japan. In the guidelines of the Japanese Society of Sexually Transmitted Infections, only parenteral regimens of ceftriaxone, cefodizime, and spectinomycin are recommended for gonococcal urethritis or cervicitis [18]. However, a national surveillance had not yet been performed in Japan [19]. There have been some reports by different testing laboratories regarding the antimicrobial susceptibility of *N. gonorrhoeae* in domestic areas [12, 13]. However, our report represents the first national surveillance performed with prospective planning

with specimens collected from multiple facilities that were tested in a single laboratory.

The prevalence rates of PPNG were 0.9 % in 2006 [1] and 0 % in 2009 [2] in Japan. However, the rate of β-lactamase-producing strains found in this study, which was 7.2 %, was higher than that in previous reports. The prevalence rate of the CMRNG strains was similar to that of previous reports. According to this study, the rate of resistance to penicillin G has also increased. In Japan, single antimicrobial therapy with penicillin for *N. gonorrhoeae* has not been used. The incursion of PPNG from neighboring countries may occur, but we have no evidence supporting such an incursion. Recently, *N. gonorrhoeae* strains with a TEM-type β-lactamase gene were found in Thailand [20]. The increase in PPNG and the appearance of the TEM-type β-lactamase gene in *N. gonorrhoeae* might conjure for us an image that a newer type of resistance such as extended-spectrum β-lactamase-producing *N. gonorrhoeae* is spreading in Japan. However, we hope this is just an imaginary spectre.

In 2009, a ceftriaxone-resistant *N. gonorrhoeae* strain (H041) was found in Kyoto, Japan [8, 21]. The specimens used in this study were collected during the same time period as when H041 was isolated, but we did not identify a ceftriaxone-resistant strain in this study. The MIC for ceftriaxone in all the strains was <0.25 μg/ml, which is included in the susceptible criteria according to the CLSI document. However, seven strains had a MIC of 0.125 μg/ml, and these strains were considered to be less susceptible. It has been reported that almost two-thirds of *N. gonorrhoeae* strains with a MIC of 0.125 μg/ml for ceftriaxone also have a *penA* mosaic, which is related to cephalosporin resistance [21, 22]. Only one strain was resistant to cefixime according to the CLSI document (MIC 0.5 μg/ml). Deguchi et al. [6, 23] recommended that the breakpoint MIC for cefixime should be changed to ≤0.06 μg/ml because the clinical efficacies of cefixime regimens were not good in Japan, and it has been found that the increase in the MIC of cefixime was also related to the *penA* mosaic [7, 22]. If the breakpoint MIC of cefixime was determined as ≤0.06 μg/ml according to Degchi's papers, the susceptibility rate for cefixime was 55.4 % in this study.

The *penA* mosaic in *N. gonorrhoeae,* which is closely correlated with resistance to cephalosporins, may be associated with *Neisseria* species found in the oral cavity. The ceftriaxone-resistant *N. gonorrhoeae* strain H041 was isolated from the pharynx of a female commercial sex worker who provided only oral sex. In addition, oral sex is very common between heterosexual couples in Japan as well as homosexual couples. In our study, *N. gonorrhoeae* was detected from the pharynx of 20 % of the heterosexual men who had gonococcal urethritis by nucleic acid amplification tests [24]. Muratani et al. [25] showed that a single dose of 1 g ceftriaxone could eradicate *N. gonorrhoeae* in the pharynx. However, a ceftriaxone-resistant strain was isolated from the pharynx of a woman who was treated with 1 g ceftriaxone.

The rate of resistance to fluoroquinolone was 78.3 %, which is similar to that of previous reports [10]. The antimicrobial susceptibility to fluoroquinolone had a completely bimodal distribution. Eighteen strains with MIC ≤ 0.06 μg/ml can be determined susceptible to ciprofloxacin and levofloxacin. However, it was surprisingly that 30 strains had MIC ≤ 0.06 μg/ml for sitafloxacin and other strains had a lower sitafloxacin MIC. If the value of ≤ 0.06 μg/ml is assumed as the breakpoint MIC of sitafloxacin, at least 12 strains that were resistant to ciprofloxacin or levofloxacin were susceptible to sitafloxacin. Among the 6 strains with a MIC of 32 μg/ml for ciprofloxacin, the MIC of sitafloxacin was 0.125 μg/ml in 3 strains and 0.25 μg/ml in the other 3 strains. In *Escherichia coli*, sitafloxacin showed strong activity against fluoroquinolone-resistant strains that had mutations in gyrase genes [26]. There has not been a clinical trial for the treatment of gonococcal infection with sitafloxacin, but these results suggest this drug could be an option.

Regarding azithromycin resistance, the MIC of two strains was 2 μg/ml, which is thought to indicate resistance to azithromycin. In Japan, a 2 g azithromycin dose is accepted by the national insurance for the treatment of *N. gonorrhoeae,* but not in the guideline of Japanese Association of Sexually Transmitted Infection. Therefore, we must carefully evaluate the susceptibility of *N. gonorrhoeae* strains to azithromycin.

Table 3 shows the patterns of combined antimicrobial resistance. Among the 65 strains that had MICs ≥ 2 μg/ml for ciprofloxacin, 27 were resistant to penicillin G, 15 were not susceptible to cefpodoxime, 1 was resistant to azithromycin, and 22 were resistant to only ciprofloxacin. Considering all the strains, 51.8 % were resistant to more than two antimicrobials, and 25 % were resistant to more than three antimicrobials. However, 18 strains with MICs ≤0.06 μg/ml for ciprofloxacin were not highly resistant to other antimicrobials. This result indicates that multidrug-resistant *N. gonorrhoeae* are fluoroquinolone resistant. Only one strain was susceptible to fluoroquinolones, penicillin G, oral cephalosporins, minocycline, and spectinomycin.

A new antimicrobial surveillance initiative for *N. gonorrhoeae* was started in Japan in 2012. Since that time, reports of gonococcal infection have decreased, and the collection of specimens has also decreased. The purpose of the new surveillance initiative is to track cephalosporin resistance and azithromycin resistance after the implementation of coverage of a single 2-g dose of azithromycin for *N. gonorrhoeae* infection by the Japanese national insurance.

Conclusion

The first national surveillance of the antimicrobial susceptibility of *N. gonorrhoeae* was performed. Multidrug resistance was found in 51.8 % of the tested isolates, and all these isolates were resistant to ciprofloxacin. Fluoroquinolone resistance was found in 78.3 % of the tested isolates, and penicillin resistance, including PPNG and CMRNG, was observed in 34.7 % of the isolates. In this study, ceftriaxone-resistant strains were not found, but the susceptibility rate for cefixime was 55.4 % even though the threshold MIC for this antibiotic is considered to be less than 0.06 μg/ml. Currently, *N. gonorrhoeae* is one of the most difficult bacterial infections to treat in Japan. The surveillance of *N. gonorrhoeae* for antimicrobial susceptibility should be continued.

Conflict of interest Akira Watanabe is a consultant to Daiichi-Sankyo, Mitsubishi Tanabe Pharma Corporation, Toyama Chemical, and Otsuka Pharmaceutical. A.W. has received a speaker's honorarium from MSD Japan, Glaxo SmithKline K.K., Shionogi & Co. Ltd., Daiichi-Sankyo, Taisho Toyama Pharmaceutical, Dainippon Sumitomo Pharma and Pfizer Japan Inc.; and grant support from Kyorin Pharmaceutical, Shionogi & Co. Ltd., Taisho Pharmaceutical, Toyama Chemical, Daiichi-Sankyo, Dainippon Sumitomo Pharma, Taiho Pharma, and Meiji Seika Pharma. Keisuke Sunakawa has a research grant for other research than this study from Meiji Seika Pharma Co., Ltd.

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Key words
性感染症
中高生
予防啓発
標準スライド
認定制度

小児保健

中高生に向けた性感染症予防の啓発活動

――学会標準版スライドの活用――

荒川創一（あらかわ そういち）*

要旨　性感染症の蔓延を防ぐ最大の防波堤は，若者への教育啓発である．sexual debut 前の中3～高1を対象とするのが，効果的と考える．本稿では，日本性感染症学会と日本思春期学会とで作成した啓発用の標準スライドの骨子を紹介しつつ，教育のポイントについて述べる．性を考えることは人生を考察することに他ならない．性教育の重要な一部を占めるのが性感染症予防啓発授業である．筆者が行ってきたデリバリー授業の理解度の集計も示す．小児科医もこの分野で重要な役割を担っている．日本性感染症学会では，認定医，認定士制度を設けて，予防啓発の実を挙げることを事業の一つと位置付けている．

はじめに

性感染症は予防できる．そして，性感染症予防は，次代を担う若者（健康な子どもを産み育み世の中に送り出す役割を担う）においてもっとも重要である．若者を性感染症から守るにはどうすればよいのであろうか．日本性感染症学会は日本思春期学会との共作により，中高生指導用の性感染症予防啓発標準スライド（パワーポイント）を作成した．また日本性感染症学会では全学会員にCDを配布した．このCDには，日本性感染症学会雑誌の性感染症病変図説（写真）（抜粋）も添付している．日本思春期学会では，同じものをホームページの学会員専用サイトにアップロードしている．筆者は，このスライド作成に携わった者の一人として，また，毎年，近隣の高等学校に出向いて高校1年生を対象の中心に予防啓発授業を担当している立場から，性感染症予防のあるべき方策について述べてみたい．

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I 性欲の目覚めへの対処

知徳教育の目的は，理性と知性を磨くことにより，将来一人前の大人として揺るぎない判断ができる人間を形成することにあると考える．しかし，同時に豊かな感情を育て，喜怒哀楽を理解しまたそれらを自己コントロールできる能力開発も重要である．一方，ヒトも動物の仲間であり，食欲に始まるともすればコントロールの困難ないわゆる「本能」を持ち合わせている．言わずもがな性欲においてもまた，コントロールの域を超えた発露となってしまったときに人間の自己抑制の困難さを垣間見てしまう現実がある．教育の場である学校で性欲の目覚めを客観的に教え，直情行為に走らず，いかにそのエネルギーを他に転じ，「精力善用」たらしめるか．それは思春期を迎えた男女（とくに能動的な性

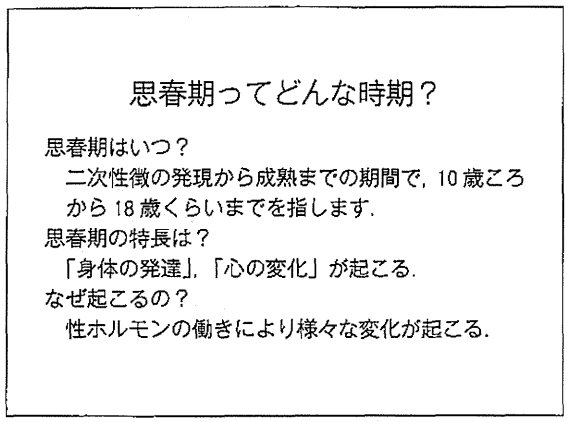

図1　思春期の説明

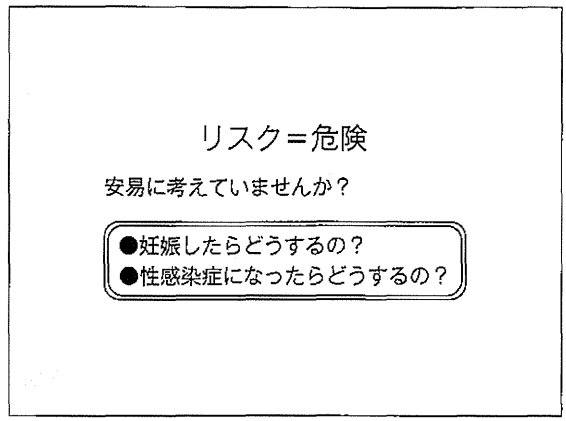

図2　性交渉のリスク指摘

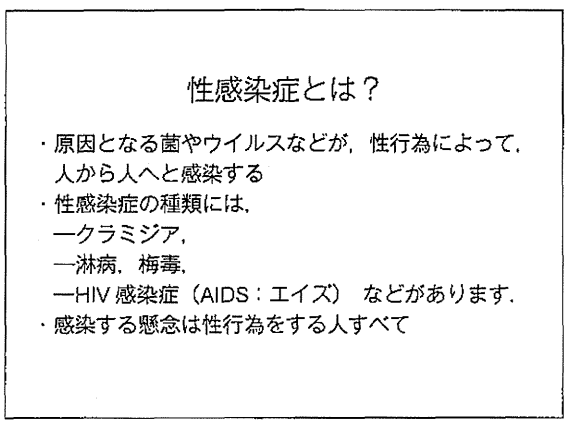

図3　性感染症とは

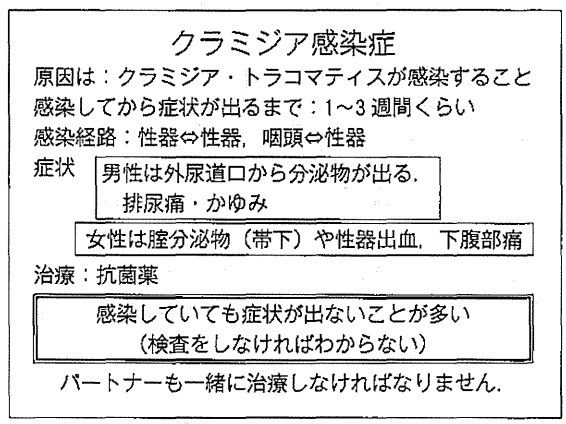

図4　クラミジア感染症とは

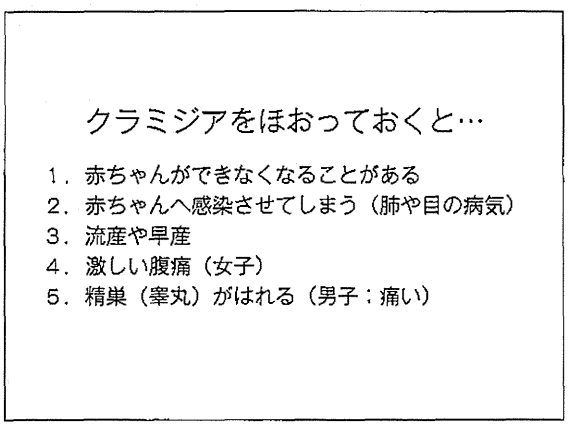

図5　クラミジア感染症の招くリスク

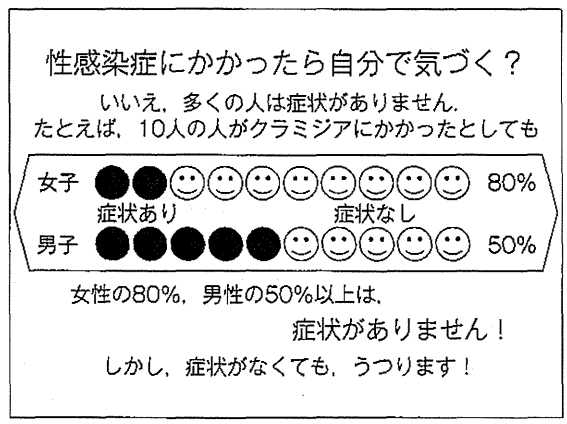

図6　性感染症の症状

の主体である男子)の抱えた課題の一つであり，古今東西のこの普遍的命題に教育がどこまで手をさしのべられるかということにも模範回答はない．しかし，ここに一つのブレーキが提示されうる．それが妊娠というリスクであり，性感染症というリスクである．教育者や医療者は，彼ら思春期の中に身を置く若者に必然的に起こってくる性欲が行為までに至った際に起こりうるいわばadverse event（有害事象）を教示し，熱く沸く感情に冷や水をかけることをある程度積極的に行わざるをえない．それは決して脅しというものではなく，scientific society（科学的社会）では常識として伝達すべき事項である．これは性教育の中の性感染症予防教育というべき一単元と捉えるべきである．

Ⅱ 具体的な性感染症予防教育の流れ（対高校生）

①．序（図1）

授業対象となる中高生が今，人生のどういう時期にいるのかということ，また思春期に起こることを具体的に説明し，男女の体型が変わってくることなどにも触れる．

②．性交渉のリスクの提示と授業の主題（図2）

望まざる妊娠と性感染症という，adverse event（有害事象）の存在を指摘．授業では，adverse event(有害事象)という言葉は使わず，“リスク”という語を使用する．

③．性感染症の具体的説明（図3～5）

具体的疾患（たとえば，性器クラミジア感染症）の症状や感染経路などを解説．無自覚に進展して女子では不妊症や子宮外妊娠の原因となることや流産・早産，垂直感染の問題，男子では精巣上体炎について説明する．

④．無症候性感染が多いことへの警鐘（図6）

ここでもクラミジア感染などを例に挙げて，症状がないまま伝播していく問題を教える．

⑤．エイズの問題の指摘（図7）

この感染症の本態や経過を理解させ，日本で年々，HIV感染症・エイズ患者が増加していることについてデータをもとに説明する．

⑥．ヒトパピローマウイルス（HPV）感染と子宮頸癌との関係（図8）

20代の若年女性の子宮頸癌が増加傾向にあることを認識させ，その背景に高リスク型HPV感染が存在すること，すなわち，子宮頸癌の多くも広い意味での性感染症であることを解説する．

⑦．性パートナーが一人であれば安心か（図9）

実際は否である．相手が一人でも，その背後に性のネットワークが存在し，感染する懸念がある．

⑧．では，どうすればいいのか（図10，11）

予防が第一である．no sexも一つの予防．あえてセックスするなら必ずコンドームを使うこと．コンドームの正しい付け方は常識として教える．もし，感染している心配があるなら，保健所で無料・匿名でHIVの検査が受けられることを伝える．

⑨．最後にメッセージ

性交を焦る必要はない．心のつながりを大切にして，ゆっくりと時間をかけて「人間関係」を築くよう伝える．まずは心のコミュニケーションを．

Ⅲ この性感染症予防教育は大人にも通じる（図12）

大人でも，性感染症の正しい知識を有している者は必ずしも多くない．「もし，あえてセックスをするのなら→必ずコンドームを使うこと(ピルなどの適切な使用も，医療機関で相談すること)．コンドームなどを使わずにセックスをしてもよいのは，互いに感染がないとき，愛する相手との間に子どもを産み，育てることができ，しかも相手もそれを望みかつ，それができる条件が整っているときだけです」という結論は，大人にも訴えたい．

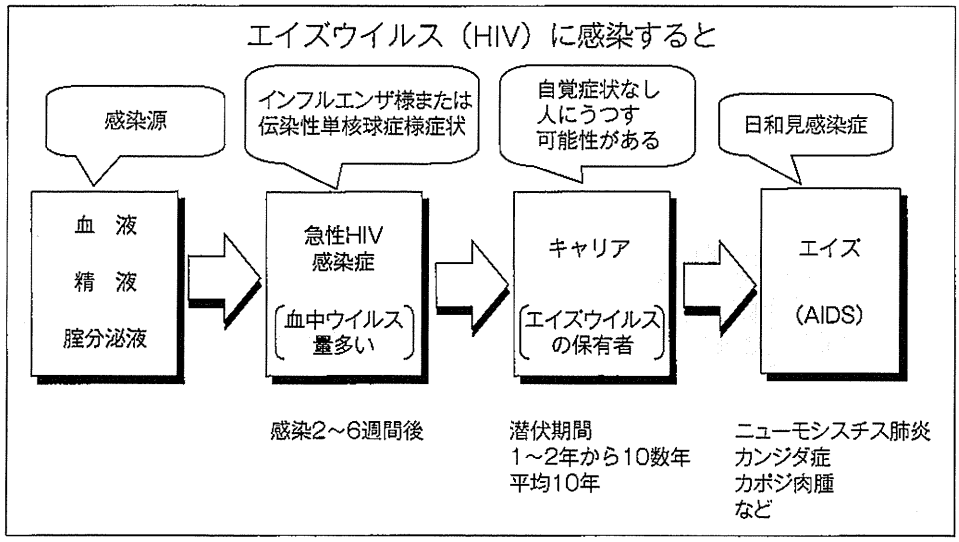

図7　エイズウイルスとは

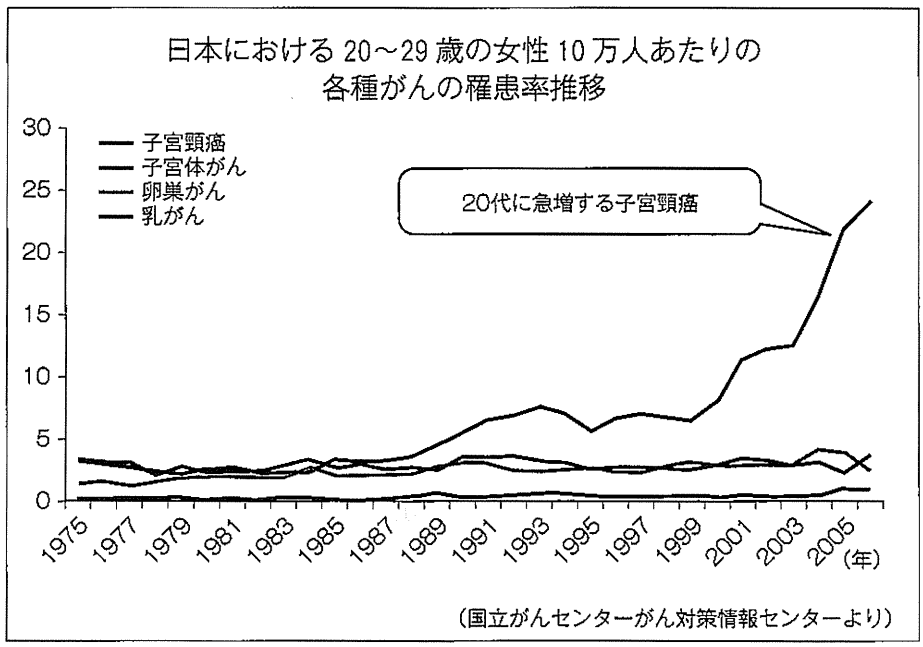

図8　20代に子宮頸癌は急増する

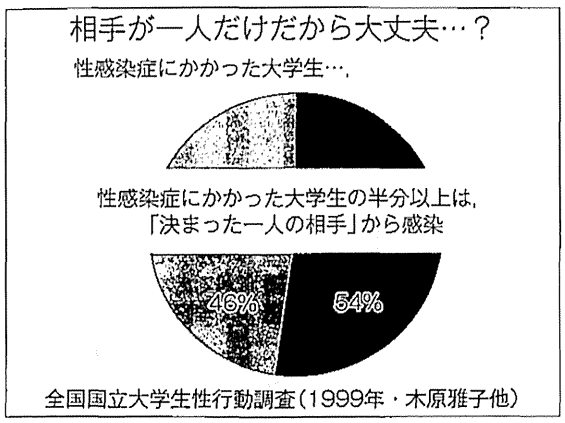

図9 性パートナーが一人のみである人の割合

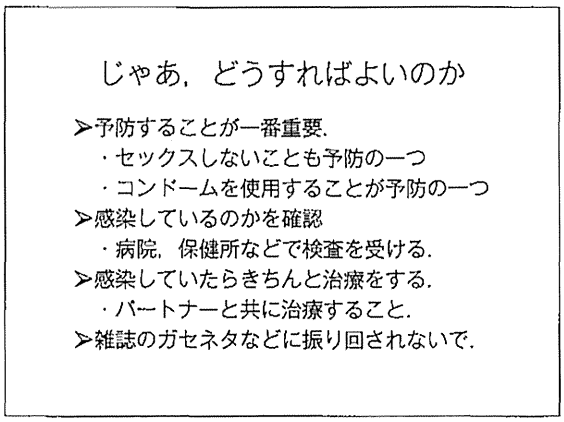

図10 性感染症に悩まないために

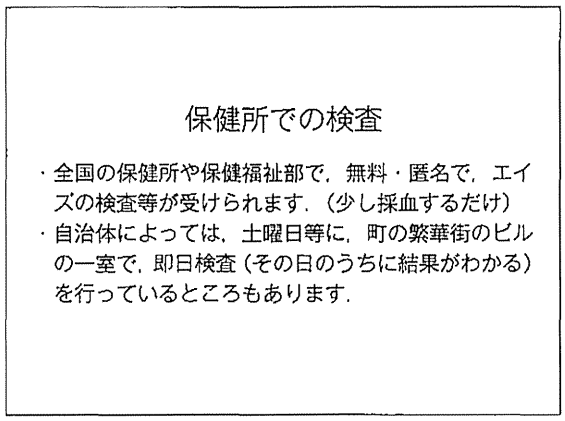

図11 検査実施施設

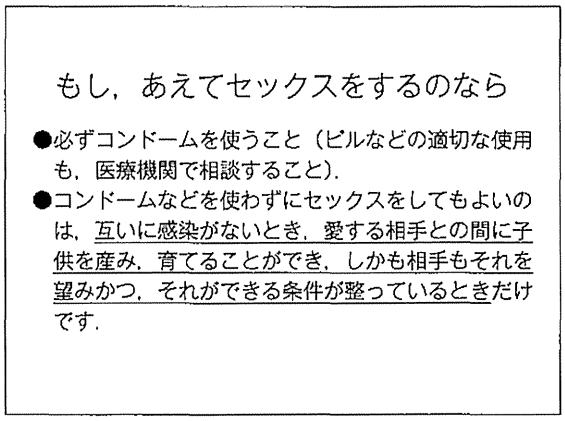

図12 大人にも通じる予防教育

Ⅳ 授業の理解度

筆者は，これらのスライドを使って，2006～2010年の5年間に神戸市内男女共学高校1～2年（もっとも多い年で7校，少ない年で4校）にデリバリー授業をした．その授業の直後に生徒からとった無記名アンケートの集計結果を図13～17に示す．おおむね，理解度は良好である．図15（設問3）にある高校生の性行為に対しての考え方はさまざまであり，「考えたことがない」と答えた生徒も多かった．また，神戸市では，中学3年時にも性感染症の授業を行っているが，多くの生徒がそのことを覚えており，2段構えの教育体制は意義があるものと思われた．

おわりに

HIV感染症の増加などの現状に照らし，中高生への性感染症の正確な知識の伝達は社会的にみて，非常に重要な課題である．日本性感染症学会では性感染症認定医（表1，細則は文献3）参照）および認定士（表2，細則は文献4）参照）制度を2009年度に発足させた．2012年までの4回の認定作業で，認定医は370名あまり誕生しているが，認定士がいまだ20名程度と少な

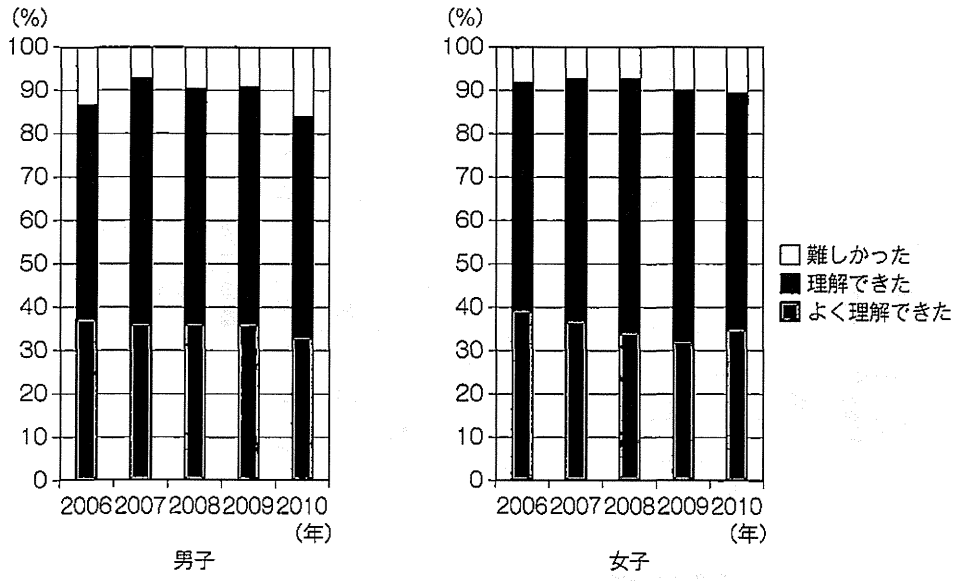

図 13　設問 1：講演会の内容が理解できましたか

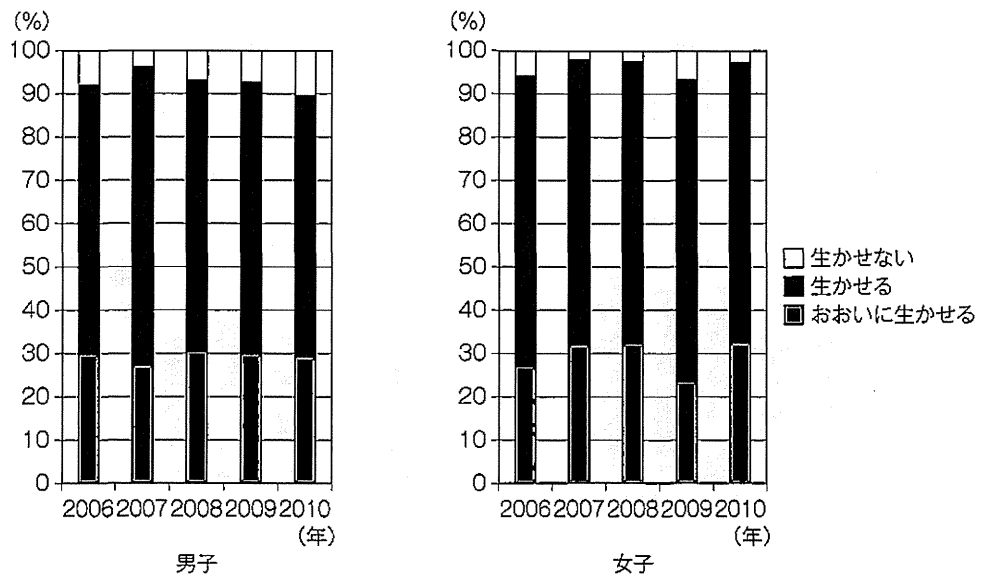

図 14　設問 2：自分の今後の性行動に生かせると思いましたか

い．今後，認定士の応募が増え増員され，日本各地区で中高生への性感染症教育を担当することにより，その推進を期待するものである．少子高齢化社会の中にあって，性感染症は日本民族にとっては脅威である．すなわち，クラミジア→不妊，HPV→子宮頸癌など，少子社会にさらにネガティブな要素をもたらす無症候性感染の怖さを，もっと社会が理解するべきである．10 代半ばでの学校現場における教育が最大の防波堤であり，教育現場と医療者の協調が必要

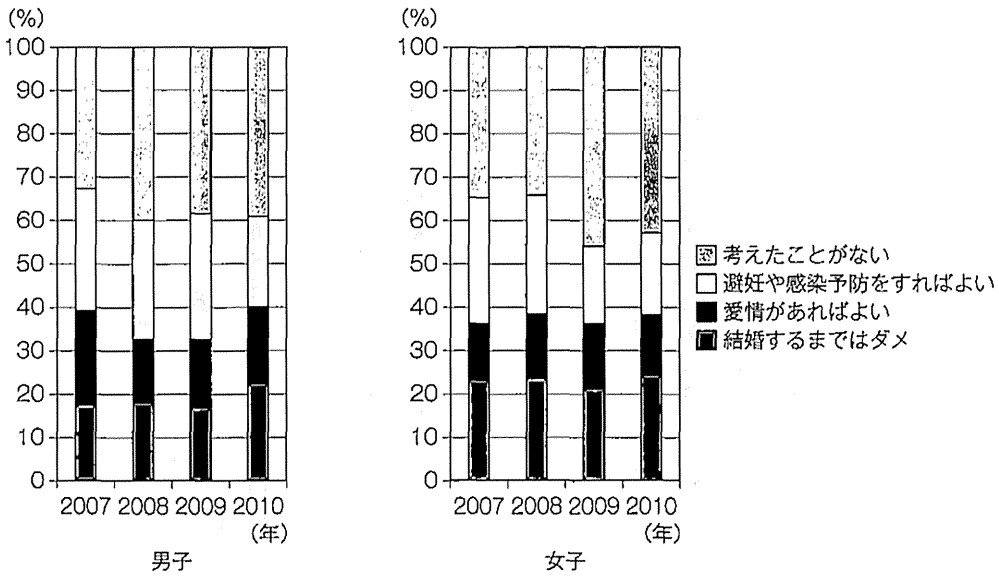

図 15　設問 3：高校生の「性行為」に対して，あなたはどう思いますか

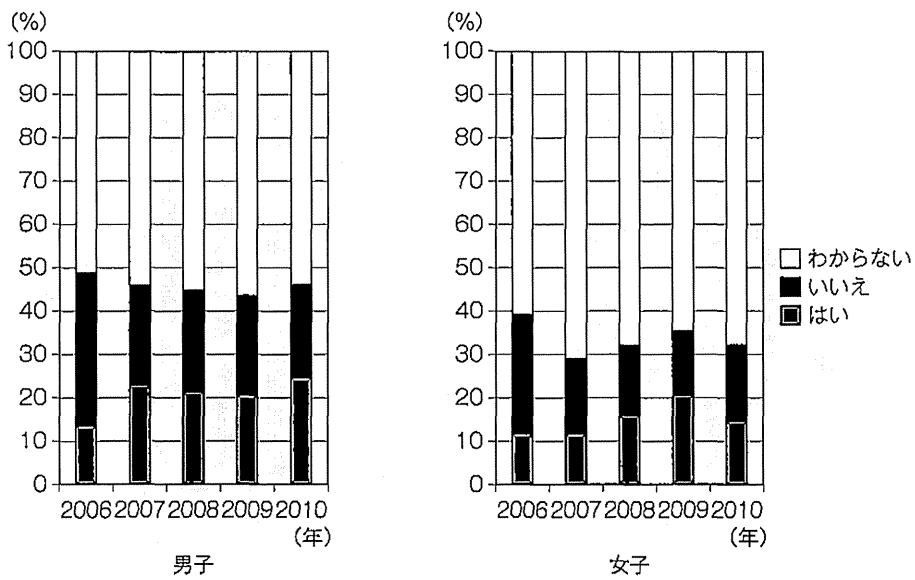

図 16　設問 4：今後，機会があれば「性感染症」の検査を受けますか

である．

感染症学と疫学とのドッキングにより，詳細な実態調査が継続的に行われ，それが国民・若者に広報され，有効な対策がとられるべきである．日本性感染症学会が，その橋渡し役を担い，認定士制度等の意義を深め，標準教育用スライドが活用されることが期待される．

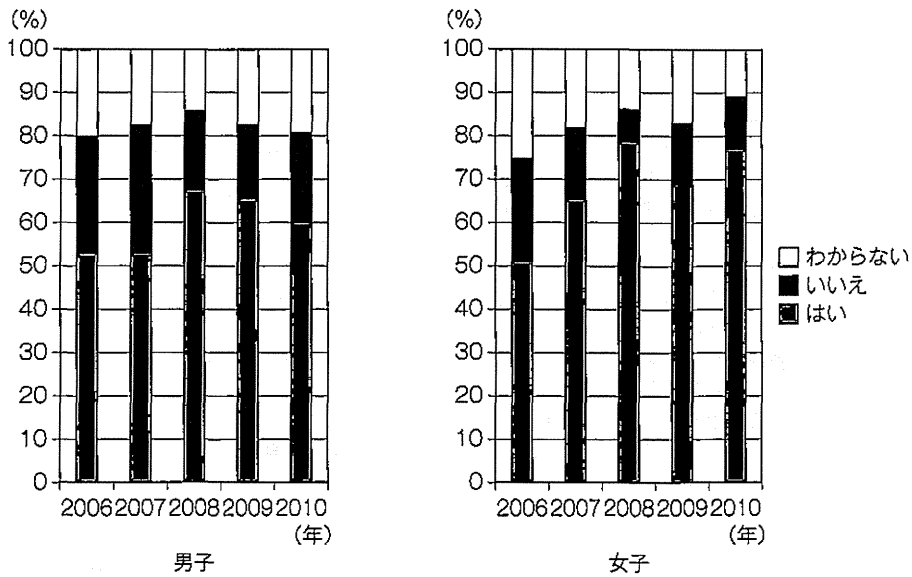

図 17　設問 5：中学生の時に，今回のような医師や助産師による性教育講演会を聞いたことがありますか

表 1　認定医制度規則

日本性感染症学会 認定医制度規則

第 1 章　総　則

第 1 条　日本性感染症学会（以下，本会という）は，性感染症の病態解明，予防，診断および治療の進歩に即応した優秀な医師の養成をはかることにより，国民の衛生，福祉に貢献することを目的として，日本性感染症学会認定医（以下，認定医という）制度を設ける．

第 2 条　本会は，前条の目的を達成するため，本会内に認定医制度委員会を置く．

第 2 章　認定医制度委員会

第 3 条　認定医制度委員会（以下，委員会という）は，第 1 条に掲げる目的を達成するために必要な事項を取り扱う．

第 4 条　委員会の委員（以下，委員という）は，常任理事会の議を経て，理事長が指名する本会理事及び代議員各若干名をもって構成する．

第 5 条　委員会の委員長（以下，委員長という）は，委員の互選により選出する．委員長は，委員会を招集し，本制度の円滑な運営を図る．

第 6 条　委員の任期は 2 年とし，2 期までの再任は妨げない．

第 7 条　委員会には，業務の運営に必要な各種小委員会をおくことができる．

第 8 条　委員会の事務は，日本性感染症学会事務局が取り扱う．

第 3 章　認定医の資格

第 9 条　認定医の資格を申請するものは，次の各項の条件を満足していなければならない．

1．日本国の医師免許証を有すること．

2．申請時において，3 年以上，本会の会員であること．

3．日本内科学会において定められたいずれかの認定医，日本泌尿器科学会専門医，日本産科婦人科学会専門医，日本皮膚科学会専門医，日本小児科学会専門医，日本耳鼻咽喉科学会専門医，日本眼科学会専門医であること，または委員会が性感染症と関連が深いと認める学会の認定医あるいは専門医の資格を有し，5 年以上，性感染症に対する基礎的研究または臨床の経験を有すること．ただし，これらに該当しない場合でも，性感染症に対し十分な臨床経験を 5 年以上積んでいると判断される者は，委員会の議を経て，同等の資格を有するものとみなすことができる．

4．本会の定める教育研修の必要単位を取得していること．〔細則§1 参照〕

5．本会が行う認定医資格試験に合格していること．〔細則§2 参照〕

（文献 3）より引用）

表2 認定士制度規則

日本性感染症学会 認定士制度規則

第1章 総 則

第1条 日本性感染症学会（以下，本会という）は，性感染症の相談・検査，予防・啓発等に携わることにより，国民の衛生，福祉に貢献することを目的として，日本性感染症学会認定医（以下，認定医という）制度とともに，日本性感染症認定士（以下，認定士という）制度を設ける．

第2条 本会は，前条の目的を達成するため，本会内に認定士制度委員会を置く．

第2章 認定士制度委員会

第3条 認定士制度委員会（以下，委員会という）は，第1条に掲げる目的を達成するために必要な事項を取り扱う．

第4条 委員会の委員（以下，委員という）は，常任理事会の議を経て，理事長が指名する本会の理事及び代議員各若干名をもって構成する．

第5条 委員会の委員長（以下，委員長という）は，日本性感染症学会認定医委員会委員長が兼務する．委員長は，委員会を招集し，本制度の円滑な運営を図る．

第6条 委員の任期は2年とし，2期までの再任は妨げない．

第7条 委員会には，業務の運営に必要な各種小委員会をおくことができる．

第8条 委員会の事務は，日本性感染症学会事務局が取り扱う．

第3章 認定士の資格

第9条 認定士の資格を申請するものは，次の各項の条件を満足していなければならない．

1．薬剤師，保健師・助産師・看護師，学校教諭・養護教諭，臨床検査技師等の日本国内の公的資格を有する者．ただし，これらに該当しない場合でも，性感染症の相談・検査，予防・啓発等に関し十分な経験を5年以上積んでいると判断される者は，委員会の議を経て，同等の資格を有するものとみなすことができる．

2．申請時において，3年以上，本会の会員であること．

3．性感染症に関する相談・検査，予防・啓発等の経験を有すること．

4．本会の定める教育研修の必要単位を取得していること．〔細則§1参照〕

5．本会が行う認定士資格試験に合格していること．〔細則§2参照〕

（文献4）より引用）

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4) 日本性感染症学会認定士制度規則
http://jssti.umin.jp/pdf/cm_bylaw.pdf

JOURNAL OF FOOD AND DRUG ANALYSIS 21 (2013) S33–S36

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Current status of substance abuse and HIV infection in Japan

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Keywords:
Evasive drugs
HIV
Homosexual transmission
Methamphetamine
Synthetic cannabinoids

ABSTRACT

Japan has experienced an epidemic of methamphetamine (MAP) abuse three times: the first epidemic was from 1951 to 1957, the second epidemic was from 1970 to 1994, and the third epidemic started in 1995 and continues today. Fortunately, HIV infection is not as serious a problem in Japan as it is in other countries. The major route of HIV infection in Japan has been through male homosexual transmission. In cumulative numbers, homosexual transmission accounted for 63% of the 11,146 HIV-positive patients and 40% of 5158 AIDS patients as of December 30, 2011. Intravenous drug use accounted for 0.3% and 0.4% of these cases, respectively. Drug abuse has changed during the past 20 years in Japan. The changes are summarized as follows: there has been: (1) a remarkable decrease in solvent abuse; (2) a stabilization of MAP abuse; (3) a penetration of cannabis abuse; (4) an emergence of evasive drug abuse; and (5) a silent increase in medical drug dependence. This implies that: (1) there has been a change from a "solvent dominant type" of use to a "cannabis dominant type," that is, from a "Japanese type" to a "Western type"; (2) a shift to drugs which do not have a high potential to cause drug-induced psychosis; and (3) a shift from conduct that leads to arrest to conduct that does not lead to arrest. Regardless of whether the drug use is illicit or not, drug dependence is a mental disorder. Japan is urged to deal with drug abuse and dependence using not only the criminal model, but also the medical model.

1. Introduction

Japan is now in the 18th year of its third epidemic of methamphetamine (MAP) abuse. However, drug abuse in Japan has drastically changed in the past 20 years, which we will explain in this paper. We begin with a brief discussion of HIV infection, which is not a serious problem in Japan.

2. HIV infection in Japan

The number of HIV-positive people in Japan is very low. Fig. 1 shows the trend of HIV cases by transmission routes. Male homosexual and heterosexual transmissions have been the two main routes. In terms of injection drug use, it is not possible to show such data in Fig. 1 because there have been

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1021-9498/$ – see front matter
http://dx.doi.org/10.1016/j.jfda.2013.09.030

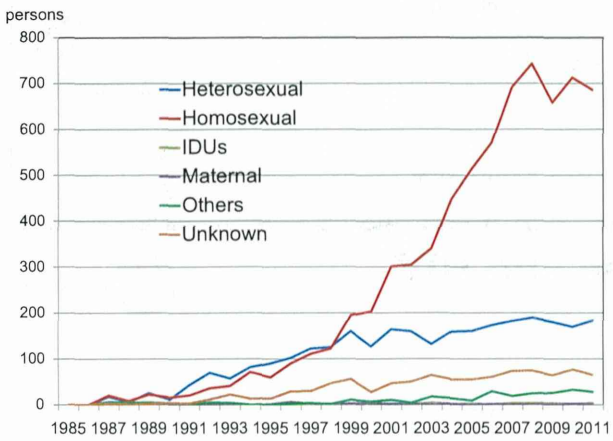

Fig. 1 – Number of HIV-positive cases (per year). Data source: the national AIDS Surveillance.

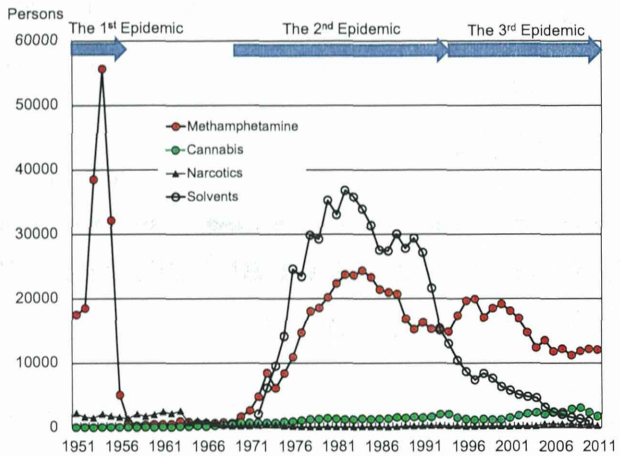

Fig. 3 – Number of arrestees by type of drug involvement. Data source: "The White Paper on Crime" and "The General Situation of Administrative Measures against Narcotics and Stimulants Abuse".

only zero to four new cases of HIV infection due to injection drug use each year.

The cumulative number of HIV-positive cases and AIDS cases among the Japanese were 11,146 and 5,158, respectively, as of December 30, 2011. Fig. 2 shows the proportion of cumulative HIV-positive patients by transmission routes. Injection drug use occupies only 0.3%. We think that this situation is caused by the fact that HIV infection among the general population is not serious and prevalence of intravenous drug use is not high in today's Japan [1].

3. Brief history of drug abuse in Japan

The history of drug abuse in Japan started after World War II and is characterized by three epidemics of MAP abuse (Fig. 3). The first epidemic was between 1951 and 1957. Under the pessimistic and pleasure-seeking atmosphere after World War II, MAP use became a social problem. The second epidemic was between 1970 and 1994. Around 1970, Japanese economic growth suddenly fell. This economic deterioration drove organized gangs to start selling MAP. The third epidemic started in 1995, after the collapse of the Japanese "Bubble Economy."

Japan's drug abuse issues are easier to understand if discussed in relation to these three epidemics of MAP abuse. For a long time, MAP and organic solvents had been clearly more problematic than other drugs in Japan [2]. MAP had been abused mainly by adults, while solvents had been abused mainly by teenagers [2]. Solvent abuse had been considered a gateway to MAP abuse in Japan [3].

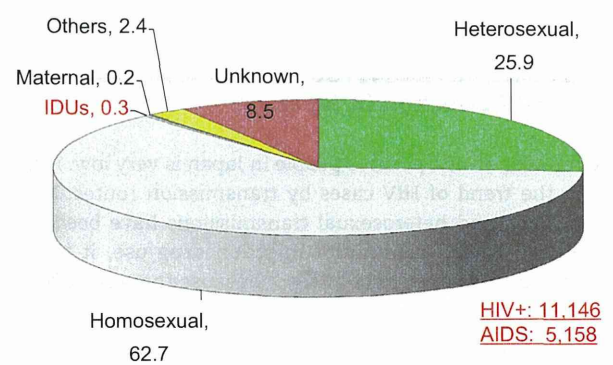

Fig. 2 – Cumulative number of HIV-positive cases (1985–2011) (%). Data source: the National AIDS Surveillance.

4. Recent drastic changes in the drug abuse situation in Japan

4.1. *From "solvent dominant type" to "cannabis dominant type"*

It has been 18 years since the third epidemic started. One noticeable change in this period is that cannabis-related arrestees outnumbered solvent-related arrestees in 2006 (Fig. 3).

According to the nationwide general population survey on drug use [2] (Fig. 4), lifetime prevalence of use of any illicit drug was 2.7% in 2011. The lifetime prevalence of organic solvent use was the highest, but does not indicate an upward trend. The lifetime prevalence of cannabis use was the second highest and indicates an upward trend. The lifetime prevalence of MAP use was the third and lowest, and the trend is stable. Therefore, we consider cannabis has being the drug with the highest prevalence of use today.

The Nationwide Mental Hospital Survey [2] indicates the change in the ratio of various "drugs as a main inducing factor" for users becoming outpatients and inpatients in mental hospitals (Fig. 5). Organic solvent and MAP use accounted for 40% of such hospitalizations in the second epidemic of MAP abuse. However, the rate of hospitalizations due to MAP use increased and those due to organic solvent use drastically decreased in the third epidemic of MAP abuse. Cannabis