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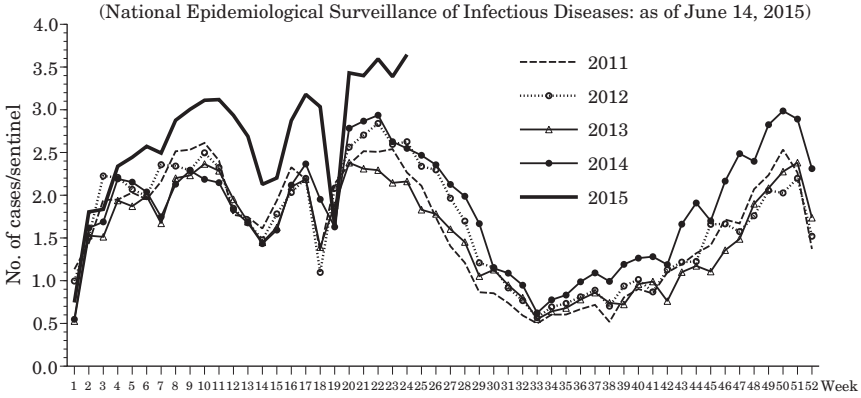
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Streptococcal Infections in Japan, 2012-2015, as of June 2015

Figure 1. Weekly number of reported group A streptococcal pharyngitis cases per pediatric sentinel, from week 1 of 2011 to week 24 of 2015, Japan
(National Epidemiological Surveillance of Infectious Diseases: as of June 14, 2015)



Many streptococci that cause suppurative disease in humans are β-haemolytic. They are classified according to the antigenicity of the cell wall polysaccharides; group A [Group A *Streptococcus* (GAS); mostly *Streptococcus pyogenes*], group B [Group B *Streptococcus* (GBS); mostly *S. agalactiae*], and group C or G [Group C or G *Streptococcus* (GCS or GGS); mostly *S. dysgalactiae* subsp. *equisimilis* (SDSE)]. GAS causes acute pharyngitis and other acute suppurative infections, such as cellulitis; scarlet fever and streptococcal toxic shock syndrome (STSS) by bacterial toxin; and rheumatic fever (see p. 160 of this issue) and acute glomerulonephritis by immunological mechanisms. GBS causes bacteremia or meningitis in neonates and sepsis or pneumonia in adults. SDSE causes septicemia and STSS in adults.

1. National Epidemiological Surveillance of Infectious Diseases (NESID)

Group A streptococcal (GAS) pharyngitis: Under the Infectious Diseases Control Law, GAS pharyngitis is a Category V infectious disease that is monitored at approximately 3,000 pediatric sentinel (see http://www.nih.go.jp/niid/images/iasr/36/426/de4261.pdf for notification criteria).

Number of cases reported annually during 2011 to 2015 was 264,043, 276,090, 253,089, 303,160 and 202,830, respectively (as of week 24 for year 2015). GAS pharyngitis exhibits seasonality and the number of patients increases from winter to spring each year (Fig. 1). In 2014-2015, the number of patients began to increase from the end of 2014 and by week 24 of 2015, the weekly report per sentinel attained the highest level (3.64) in the past 10 years (Fig. 1, see p. 149 of this issue). The cumulative reported number of patients per sentinel from the 1st week of 2014 to the 24th week of 2015 was highest in Yamagata, Tottori, Niigata, Fukuoka, Hokkaido, Ishikawa, Yamaguchi, Shimane, Kagoshima and Fukui prefectures (see p. 149 of this issue). An outbreak in a care facility was also reported (see p. 150 of this issue). In 2015 (as of week 24), 84% of the GAS pharyngitis patients were 9 years of age or younger, and 5-year-olds were the most reported age, occupying 9.4% of all reported cases.

Streptococcal toxic shock syndrome (STSS): Any GAS, GBS or SDSE can cause STSS. STSS is a Category V infectious disease that requires notification of all cases (see http://www.nih.go.jp/niid/images/iasr/36/426/de4262.pdf for notification criteria). Since April 2006, notifications include all cases in which samples from the normally sterile sites or organs were positive for any GAS, GBS or SDSE, and manifesting shock with two or more of the following: liver failure, renal failure, acute respiratory distress syndrome, disseminated intravascular coagulation, soft tissue inflammation, acute generalized exanthema and central nervous system involvements.

The number of STSS cases has been increasing since 2011; 241, 201, and 270 cases were reported in respective years from 2012 to 2014 (Table 1). In 2015, number of reported cases reached 204 within the first 24 weeks (see p. 153 of this issue). During 2012-2014, STSS was reported from all 47 prefectures in Japan; prefectures that reported more than 1 patient per 100,000 population were Toyama (1.86), Tottori (1.38), Fukui (1.13) and Ehime (1.07). Median age of patients was 67 years and male to female ratio 1.1

(Continued on page 148′)

(THE TOPIC OF THIS MONTH-Continued)

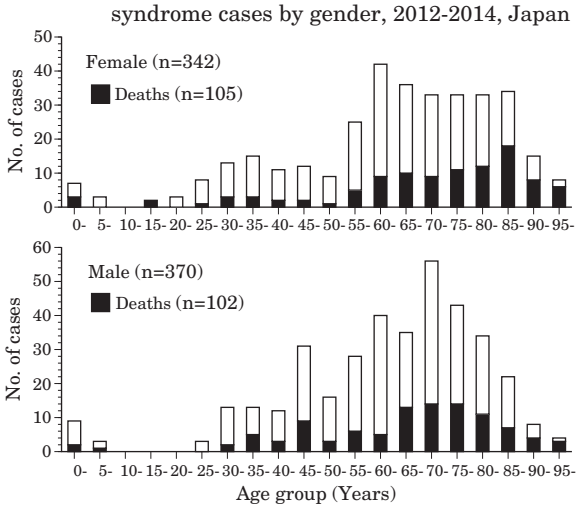
Table 1. No. of cases by serogroup of *Streptococcus* isolates from streptococcal toxic shock syndrome (STSS) cases in Japan, 2012-2014

Year of diagnosis	Serogroup*												Total	
	A		B		C		G		Others		Unknown			
2012	154	(45)	10	(5)	5	(3)	58	(18)	1	(1)	14	(2)	241	(74)
2013	114	(34)	16	(7)	5	(1)	59	(18)	–		7		201	(60)
2014	143	(34)	31	(9)	8	(3)	76	(23)	4	(3)	12	(3)	270	(73)
Total	411	(113)	57	(21)	18	(7)	193	(59)	5	(4)	33	(5)	712	(207)

No. of deceased cases indicated in parenthesis; no. of cases listed include cases from whom more than 2 serogroups were isolated.
(National Epidemiological Surveillance of Infectious Diseases: as of June 18, 2015)

(370 males vs. 342 females). Among 712 patients, 207 (29%) were deceased at the time of notification (Fig. 2). The median age of deceased patients was 72 years. Seventy-six percent of deceased patients died within 3 days after disease onset. Group A (58%) was the most frequent causative streptococci identified among STSS in 2012-2014, followed by group G (27%), which are currently increasing (Table 1).

Figure 2. Age distribution of streptococcal toxic shock syndrome cases by gender, 2012-2014, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of June 14, 2015)

2. Pathogen surveillance

Since 1992, when the first STSS case was reported in Japan, *Streptococcus* Reference Center (SRC), jointly established by prefectural and municipal public health institutes (PHIs) and the National Institute of Infectious Diseases (IASR 18: 25-26, 1997; IASR 31: 76-77, 2010; IASR 33: 211-212, 2012), has been conducting pathogen surveillance, including T-serotyping, genotyping of *emm* gene (encoding M protein responsible for pathogenicity of *S. pyogenes* and SDSE), and antimicrobial susceptibility tests.

1) T-serotyping: In 2011-2014, PHIs conducted T-serotyping for 947-1,240 isolates annually from GAS pharyngitis cases (Fig. 3a in p.149 of this issue). During 2011-2012, T1 and T12 were dominant, while in 2013-2014, T12 and TB3264 became dominant (Fig. 3a). On the other hand, among the 321 total isolates from STSS cases, T-serotype distribution (Fig. 3b in p.149 of this issue) was as follows: 153 (48%) T1, 58 (18%) TB3264, 23 (7%) T12, and 20 (6%) T28. T1 was dominant and occupied 60-70% in 2010-2011 (IASR 33: 209-210, 2012), although decreased to 26-49% in 2012-2014 (Fig. 3b). Among streptococci isolates from GAS pharyngitis and STSS cases in metropolitan Tokyo, many were similarly TB3264 in 2013-2014 (see p. 151 of this issue).

2) *emm* typing: As for *emm* typing, which can provide epidemiologically useful information, among 243 GAS isolates from STSS cases in 2012-2014, isolates with *emm1* genotype occupied 41% (100 isolates) (see p. 154 of this issue).

3) Antimicrobial susceptibility: The first choice for treating β-haemolytic streptococci infections is penicillin-derivatives. The 1,608 isolates from GAS pharyngitis patients in 13 prefectures from 2011 to 2014 were all susceptible to β-lactam antibiotics, although about 60% were resistant to macrolides and 25% resistant to lincomycin and tetracycline (see p. 152 of this issue). The recommended therapy for STSS is combination of high dose administration of penicillin-derivative antibiotics and clindamycin. The 243 isolates from STSS patients during 2012-2014 were all susceptible to penicillin G, ampicillin, cefazolin, cefotaxime, meropenem and linezolid. However, 28 isolates (12%) were resistant to clindamycin (see p. 155 of this issue).

3. Group B *Streptococcus* (GBS): GBS may cause not only STSS but also invasive streptococcal infection in neonates via vertical transmission. Recently, invasive GBS infection cases have been increasing, with the rate of invasive GBS infection among neonates within 3 months of birth in 2014 reaching 1.8 per 10,000 births (see p. 158 of this issue). Among bacterial meningitis cases reported from approximately 500 sentinel hospitals under NESID, GBS has been the most frequent (bacterial meningitis caused by *Haemophilus influenzae* and *Streptococcus pneumoniae* that had been dominant until 2011 are now monitored separately).

Recently, GBS with reduced penicillin susceptibility (PRGBS) has emerged. Among all GBS isolates, about 15% of GBS were PRGBS and 10% were PRGBS with resistance to both macrolides and fluoroquinolones (see p. 156 of this issue).

Additional comments: The reported number of GAS pharyngitis and STSS cases has been increasing in recent years. Several food poisoning outbreaks due to *S. pyogenes* have been reported (IASR 34: 266-267 & 268-269, 2013). Pediatric sentinel-based monitoring of GAS cases and notification of all STSS cases should be further strengthened. Pathogen surveillance should be further intensified by means of T-serotyping, *emm* typing and antimicrobial susceptibility monitoring. The pathogen surveillance data should be promptly fed back to clinicians so that the information can be used for understanding of ongoing streptococcal epidemics and for early diagnosis and therapy. Streptococcal infection caused by *S. suis* that claimed many lives in Southeast Asia has been reported from Japan (see p. 159 of this issue) but do not exhibit the typical β-hemolysis (IASR 26: 241-242, 2005). Paying attention to streptococci at large beyond those associated with β-hemolysis is important.

The statistics in this report are based on 1) the data concerning patients and laboratory findings obtained by the National Epidemiological Surveillance of Infectious Diseases undertaken in compliance with the Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infections, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

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＜特集関連情報＞

小児科定点疾患としてのA群溶血性レンサ球菌咽頭炎の動向（2011年～2015年第24週）

はじめに

A群溶血性レンサ球菌は，上気道炎や化膿性皮膚感染症などの原因菌としてよくみられるグラム陽性菌で，菌の侵入部位や組織によって多彩な臨床症状を引き起こす。上気道感染症については，乳幼児では咽頭炎，年長児や成人では扁桃炎が現れ，発赤毒素に免疫のない人は猩紅熱といわれる全身症状を呈することがある。気管支炎を起こすことも多い。発疹を伴うこともあり，免疫学的機序を介して，リウマチ熱や急性糸球体腎炎などの二次疾患を起こすこともある。本稿では，感染症法に基づく感染症発生動向調査において，全国約3,000カ所の小児科定点医療機関が週単位で届出を行う5類感染症の一つであるA群溶血性レンサ球菌咽頭炎の近年の動向について述べる。なお，同症の届出基準は患者（確定例）として，症状や所見から当該疾患が疑われ，かつ発熱，咽頭発赤，苺舌の必要な臨床症状をすべて満たすか，すべて満たさずとも必要な検査所見（咽頭ぬぐい液を検査材料とした菌の培養・同定による病原体の検出，あるいは迅速診断キットによる病原体の抗原の検出，あるいは血清を検査材料としたASO法またはASK法による抗体のペア血清での陽転または有意の上昇）を満たすことなどとなっている。詳細については以下のURLを参照されたい（http://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/01-05-17.html）。

発生動向

2011年～2015年第24週までのA群溶血性レンサ球菌咽頭炎患者報告数の推移を定点当たり患者報告数として本号1ページ特集の図1に示す。A群溶血性レンサ球菌咽頭炎の発生は元より季節性があり，冬から春にかけて患者数は増加するが〔Pediatrics, 2007; 120(5): 950–957〕，2014年後半より例年を超える患者の届出がみられていた。2015年に入り，その傾向は顕著なものとなり，第24週における過去5年間の患者数の比較では，＋4.09 SDの増加が観察された。第1週～24週までの累積報告数の状況を各年間で比較すると，2015年の累積報告数（全国203,639，定点当たり累積数64.73）については過去10年間で最多であり，次点となる2008年の定点当たり累積報告数（51.63），2007年の同（51.27）を大きく上回った。

地理的な分布については，2014年第1週～2015年第24週までの定点当たり累積報告数が最も多かった上位10道県は，山形県（299.00），鳥取県（293.84），新潟県（275.98），福岡県（252.55），北海道（240.42），石川県（235.86），山口県（228.24），島根県（221.66），鹿児島県（221.23），福井県（213.49）の順であった。2015年に入り，第24週までの間に定点より1万人を上回る累積報告数を寄せていた自治体は東京都（18,492），北海道（12,492），神奈川県（12,361），大阪府（12,103），埼玉県（11,632），福岡県（11,201）の順であり，大都市圏が上位を占めた。

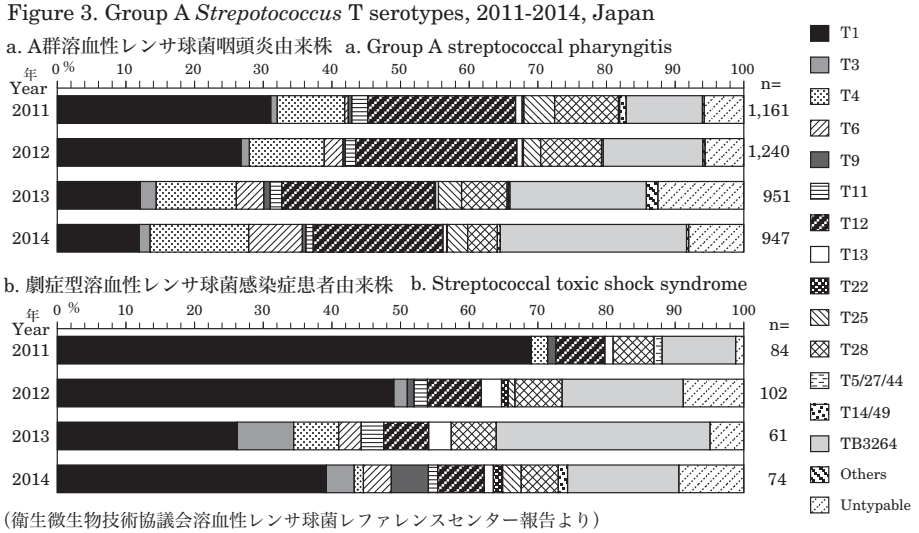
小児科の定点より報告されている2015年第24週までの累積報告数の年齢別分布については，5～9歳（50.9％），1～4歳（32.8％），10～14歳（10.6％），20歳以上（4.3％），15～19歳（0.8％），1歳未満（0.6％）の順となっており，うち5歳児が最も多い（9.4％）。

おわりに

近年のA群溶血性レンサ球菌咽頭炎の検査法，報告における小児科定点数の原則，報告基準などに変化はないことから，2014～2015年にかけての小児科定点医

（特集つづき）

図3. A群溶血性レンサ球菌T血清型別割合の推移，2011～2014年
Figure 3. Group A *Strepotococcus* T serotypes, 2011-2014, Japan



（衛生微生物技術協議会溶血性レンサ球菌レファレンスセンター報告より）
(The *Streptococcus* Reference Center, the Associations of Public Health Laboratories for Microbiological Technology)