

SHORT REPORT

Distribution of *emm* genotypes among group A streptococcus isolates from patients with severe invasive streptococcal infections in Japan, 2001–2005

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SUMMARY

We surveyed *emm* genotypes of group A streptococcus (GAS) isolates from patients with severe invasive streptococcal infections during 2001–2005 and compared their prevalence with that of the preceding 5 years. Genotype *emm1* remained dominant throughout 2001 to 2005, but the frequency rate of this type decreased compared with the earlier period. Various other *emm* types have appeared in recent years indicating alterations in the prevalent strains causing severe invasive streptococcal infections. The cover of the new 26-valent GAS vaccine fell from 93·5% for genotypes of isolates from 1996–2000 to 81·8% in 2001–2005.

Group A streptococcus (GAS) is one of the most common human pathogens and causes a wide array of infections, the most frequent of which is acute pharyngitis (strep throat). Many streptococcal virulence factors have been implicated in the pathogenesis of streptococcal infection including pyrogenic exotoxins (SpeA, SpeB and SpeC) and M protein. M protein protects GAS from phagocytosis by polymorphonuclear leukocytes [1, 2]. More than 90 of M serotypes have been identified, and a molecular approach to identification of *emm* (M protein) genes has also been

documented [3]. From the late 1980s, severe invasive infections such as streptococcal toxic shock-like syndrome (TSLS) and necrotizing fasciitis (NF) caused by GAS became a serious problem in both developed and developing countries. The first defined case of TSLS in Japan was reported in 1992 [4]. In almost all of the countries which have surveyed the prevalence of M serotypes, strains of *emm3* and *emm1* genotypes are dominant in causing severe invasive infections. In Japan, where periodic sampling surveys are performed on a 5-year cycle, *emm1* remained the most frequent from 1992 to 2000, but *emm3* strains which predominated from 1992 to 1995 decreased during 1996–2000 [5].

In this study, we report the frequency of genotypes of isolates from patients with severe invasive

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† Other group members are listed in the Appendix.

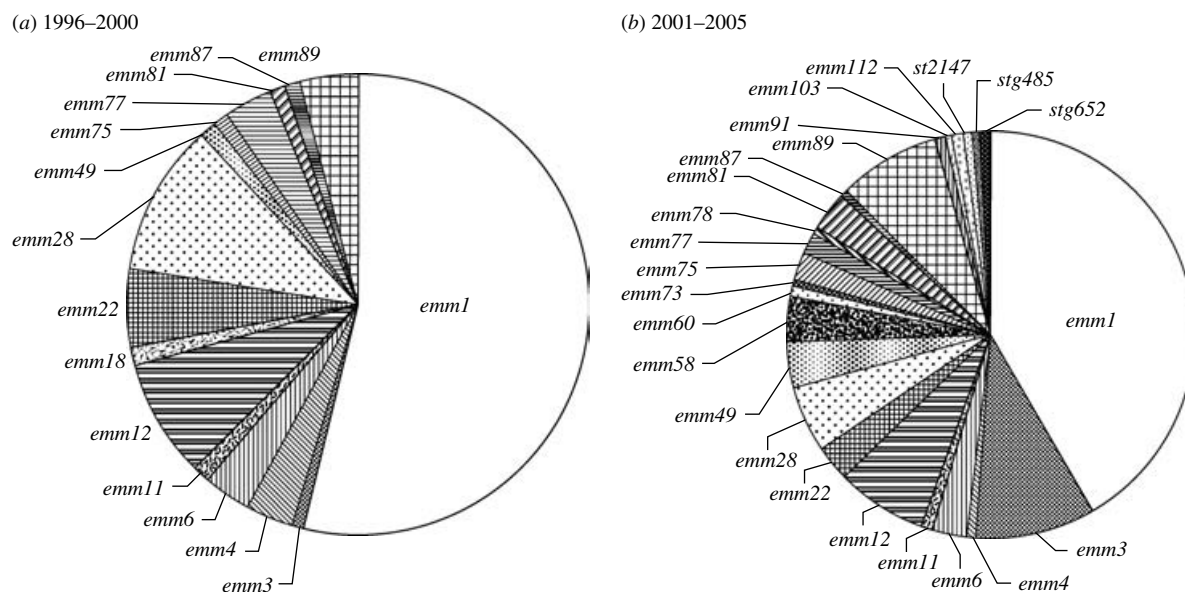


Fig. The rate of *emm* genotypes of strains isolated from patients of severe invasive streptococcal infections. (a) 1996–2000, (b) 2001–2005. (Number of each *emm* genotyped isolate during each period/number of severe invasive infections isolates during each period.)

streptococcal infections, TSLS and/or NF, from 2001 to 2005 in Japan and compare these data with the preceding sampling period from 1996 to 2000.

Information on patients with severe invasive streptococcal infections and *emm* genotypes of the isolates during the period of 2001–2005 was submitted to the National Institute of Infectious Diseases from the branch offices of reference centre and cooperative hospitals [5]. The diagnostic criteria of TSLS were based principally on those described by the Working Group on Severe Streptococcal Infections (1993) [6].

A total of 137 GAS isolates were cultured predominantly from sterile sites of patients with severe invasive infections during the period of 2001–2005. The ratio of each genotype compared between the two sampling periods is given in the Figure. Isolates of *emm1* remained dominant over the two periods, accounting for 50 out of 93 (53.8%) cases in 1996–2000 and 57 out of 137 (41.6%) cases in 2001–2005; there was a slight reduction in the ratio of *emm1* to other genotypes. On the other hand, *emm3* isolates increased dramatically from 1.08% (1/93) to 9.49% (13/137) ($P < 0.01$). It is noteworthy that this genotype was already prevalent (33%) among TSLS isolates more than 10 years previously [5] and despite the marked decrease in the 1996–2000 sampling period, its prevalence is clearly increasing in more recent years. Fewer than seven *emm* genotypes were isolated each year in 1996–2000, while 8–15 *emm* genotypes were

recorded in the subsequent years. A total of 15 *emm* genotypes were isolated during 1996–2000 compared with 23 *emm* genotypes in the later period; 10 genotypes (*emm58*, *emm60*, *emm73*, *emm78*, *emm91*, *emm103*, *emm112*, *st2147*, *stg485* and *stg652*) were isolated from patients in the later period but were absent in the first sampling period (Fig.). These results indicate the change and diversity of genotypes over time in Japan.

On the basis of epidemiological data demonstrating that the majority of non-invasive and invasive streptococcal infections are caused by a limited number of M-types, a multivalent vaccine containing amino-terminal fragments of M proteins from 26 different serotypes of GAS has recently been developed in the United States [7]. Based on the seroprevalence data presented here for Japanese GAS from invasive disease the vaccine would provide cover for 87 out of 93 strains (93.5%) isolated in 1996–2000 and for 112 out of 137 (81.8%) in 2001–2005. These data therefore have important implications for the formulation and composition of candidate vaccines against streptococcal infections in Japan.

APPENDIX. Working Group for Beta-haemolytic Streptococci in Japan

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DECLARATION OF INTEREST

None.

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