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NEWS AND PERSPECTIVES

Scarlet fever outbreak in Hong Kong, 2011

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An outbreak of scarlet fever hit Hong Kong in 2011. At least 600 cases of scarlet fever have been reported in Hong Kong till the end of June 2011, with two resulting in deaths. The first fatal case, a 7-year-old girl, presented with fever, sore throat, vomiting, and skin rash on May 20. She consulted a private doctor first but her condition did not improve. She was referred and admitted to Queen Mary's Hospital on May 27. Her condition further deteriorated and complicated with toxic shock syndrome. She passed away on May 29. The second fatal case, a 5-year-old boy, presented with fever from June 15. He was admitted to Princess Margaret Hospital on June 19 for sudden deterioration in condition. The boy developed toxic shock syndrome and passed away on June 21. He had consulted a general practitioner for chickenpox earlier. Further laboratory investigation showed that the isolates of *Streptococcus pyogenes* from both fatal cases belonged to different strains. *Emm*12 and *emm*1 were identified for both *S pyogenes* isolates. University of Hong Kong scientists said that they had discovered a mutation of the main isolates, making it more contagious and deadly. The new strain was more resistant to erythromycin and clindamycin, a resistance rate increasing from 10–30% previously to 60%, by picking up one or more genes from bacteria normally found in the human oral and urogenital tracts. Because Hong Kong and Taiwan are very close, both geographical location and people, it is quite common for people living in Taiwan to travel to Hong Kong, and thus, the possibility of the mutated strain being imported into Taiwan is high. Both the health authorities and professionals should be alert on this disease and meticulously monitor the progression of this epidemic.

Group A streptococcus (GAS) (*S pyogenes*) is among the most common and versatile of human pathogens. It causes human diseases ranging from noninvasive infections, such as pharyngitis, impetigo, cellulitis, and scarlet fever, to life-threatening conditions, such as bacteremia, necrotizing fasciitis, and streptococcal toxic shock syndrome (STSS). The M protein encoded by the *emm* gene is a major virulence factor of GAS. M1, M2, M3, M4, M6, and M22 strains have been shown to be associated with outbreaks of scarlet fever.[1–4] M1 and M3 were associated with invasive disease and fatal infections in Britain from 1980 to 1990 and in the United States from 1995 to 1999,[5,6] and M18 was associated with acute rheumatic fever.[7] Nowadays, epidemiological studies usually use sequence analysis of the 5′ end of the *emm* gene to define GAS strains.

Scarlet fever is one of the most common infections caused by GAS in school children. Clinical features of scarlet fever include a sore throat, skin rash, and strawberry tongue. In Taiwan, scarlet fever was listed as a national notifiable disease till 2007. The number of cases of scarlet fever in Taiwan fluctuated yearly and had geographic variations in different parts of Taiwan. Yan et al[3] analyzed 77 GAS isolates collected from patients with scarlet fever between 1993 and 2002 in southern Taiwan and found only three *emm* types among the isolates, with *emm*1 being the most prevalent type. Later, Su et al[8] reported that *emm*12, emerging in 2005 and peaking in 2007, was the major *emm* type associated with scarlet fever between 1998 and 2007 in southern Taiwan. In northern Taiwan, Chen et al[9] characterized 830 isolates

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that were collected from the patients with scarlet fever between 2001 and 2002, and found that *emm*1 (29.2%), *emm*4 (24.1%), *emm*12 (19.0%), *emm*6 (15.8%), *stIL*103 (5.7%), and *emm*22 (1.9%) were the most frequent *emm* types. In central Taiwan, *emm*12, *emm*4, *emm*1, *emm*6, and *emm*22 were the five most common *emm* types among GAS isolates causing scarlet fever.[10,11] The geographic variation in the prevalence of *emm* clones accounted for the difference in the epidemiological trend of scarlet fever in different parts of Taiwan in different years.

Most deaths caused by GAS were because of invasive diseases. Since late 1980s, there has been a marked increase of STSS, which was associated with shock and multiple-organ failure.[12–15] A new, highly virulent subclone of serotype M1T1, being studied to evolve as a result of diversification of the bacteria and acquisition of new genes, emerged to cause severe diseases.[16] In Taiwan, Huang et al[17] reported a family cluster of STSS in children. Among adults in Taiwan, M1 serotype was significantly associated with the clinical signs of STSS and with mortality.[18] Recently, Chiang-Ni et al[19] showed that the emergence of uncommon *emm* type of GAS, including *emm*13, *emm*81, and *emm*106, was noted in patients older than 50 years and was significantly associated with a specific invasive disease manifestation in southern Taiwan. Close epidemiological and microbiological surveillance of GAS disease is warranted. Currently, there is no definitive treatment against the toxins. Treatment for STSS includes supportive hemodynamic stabilization, surgical debridement if site of infection is identified, and antibiotic therapy.[20] In addition to penicillin, clindamycin can be used to improve survival by inhibiting protein synthesis. The Centers for disease control of United States does not recommend the routine administration of chemoprophylaxis to all household contacts of the person with invasive GAS disease. Health care providers routinely inform household contacts of the person with invasive GAS disease about the clinical manifestations of pharyngeal injection and invasive GAS disease, and to seek immediate medical attention if they develop such symptoms.[21]

GAS isolates in Taiwan were susceptible to penicillin, cefotaxime, cefepime, meropenem (Sumitomo Pharmaceuticals, Tokyo, Japan), moxifloxacin (Bayer Co., Leverkusen, Germany), vancomycin (Eli Lilly & Co., Indianapolis, IN, USA), linezolid (Pharmacia, Kalamazoo, MI, USA).[22] Before 2000, the rate of macrolide resistance in GAS reached 40–60%.[23] Under a restrictive governmental policy, which has been implemented in 2001, the rate of macrolide resistance to GAS decreased to 17%.[23] A 26-valent recombinant M protein vaccine (including Types 1, 1.2, 2, 3, 5, 6, 11, 12, 14, 18, 19, 22, 24, 28, 29, 33, 43, 59, 75, 76, 77, 89, 92, 94, 101, and 104) is under clinical trials and was found to be safe and immunogenic in adults.[24] On the basis of epidemiological data, the current formulation of the experimental multivalent vaccine would provide good coverage in high-income countries where GAS diseases were caused by a limited number of seroytpes, but poor coverage in Africa and the Pacific area, and only average coverage in Asia and the Middle East. More trials are needed to prove that the multivalent vaccine is effective and could be potentially administrated to pre-school-aged children to prevent GAS diseases.

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