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$M1_{UK}$ lineage in invasive group A streptococcus isolates from the USA

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Nicola N Lynskey and colleagues[1] reported that a hypertoxigenic clone of *emm*1 group A streptococcus ($M1_{UK}$), characterised by increased streptococcal pyrogenic exotoxin A (SpeA) production, has rapidly emerged in the UK since 2014. Large-scale genomic examinations of this $M1_{UK}$ clade indicated a single lineage in the global group A streptococcus genomic databases, with only one isolate identified in the USA in 2015.[1,2] We investigated whether the $M1_{UK}$ lineage has expanded in the USA since 2015 using data from the Active Bacterial Core surveillance (ABCs) system of the US Centers for Disease Control and Prevention.

From 2015 to 2018, 7366 cases of invasive group A streptococcus infection were identified by the ABCs system, and 6335 (86·0%) isolates were characterised by whole-genome sequencing.[3] Among the characterised isolates, 1052 (16·6%) were *emm*1. Mapping the sequencing reads against the M1 reference genome MGAS5005[4] identified ten isolates carrying all 27 single-nucleotide polymorphisms (SNPs) unique to the $M1_{UK}$ lineage and one isolate carrying 26 of these SNPs. The 11 isolates ($M1_{UK\_USA}$) clustered together with $M1_{UK}$ isolates randomly selected with R software (version 3.4.3) from a previous molecular mapping study[1] (figure), and their distances to the most recent common ancestor ranged from six to 23 SNPs. Analysis of phylogeny temporal structure suggested the ancestor had originated around June, 2012. Three $M1_{UK\_USA}$ isolates from New York state in 2016 differed from each other by a maximum of three SNPs, consistent with close transmission links within a disease cluster.

Between 2015 and 2018, the numbers of $M1_{UK\_USA}$ group A streptococcus isolates (and proportions of total *emm*1) identified each year were one of 308 (0·3%), seven of 254 (2·8%), none of 312 (0%), and three of 178 (1·7%), respectively. We found no evidence of $M1_{UK\_USA}$ lineage expansion in the ABCs system (Cochran-Armitage test, p=0·36). The 11 $M1_{UK\_USA}$ group A streptococcus isolates were observed in six different states, and in each state the lineage was seen only in a single year (figure). Syndromes caused by the $M1_{UK\_USA}$ lineage in patients were cellulitis (four patients), pneumonia (three patients), primary bacteraemia (one patient), necrotising fasciitis (one patient), streptococcal toxic shock syndrome (one patient), septic shock (one patient), septic arthritis (one

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patient), empyema (one patient), and abscesses (one patient). Three (27·3%) of the 11 patients infected by the $M1_{UK\_USA}$ lineage died (one with primary bacteraemia, one with streptococcal toxic shock syndrome, and one with septic shock), two of whom were within the New York cluster. This case fatality ratio was higher than that observed among patients infected by non-$M1_{UK\_USA}$ *emm*1 group A streptococcus (160 [15·4%] of 1041), but the difference was not significant (Fisher's exact test, p=0·39).

In summary, the $M1_{UK}$ lineage was seen in diverse geographic regions, formed a local disease cluster, and caused severe infection syndromes in the USA from 2015 to 2018. Although this clone did not expand substantially according to data in the ABCs system, continued genomic surveillance is needed to monitor the effects of this and other emerging virulent strains.

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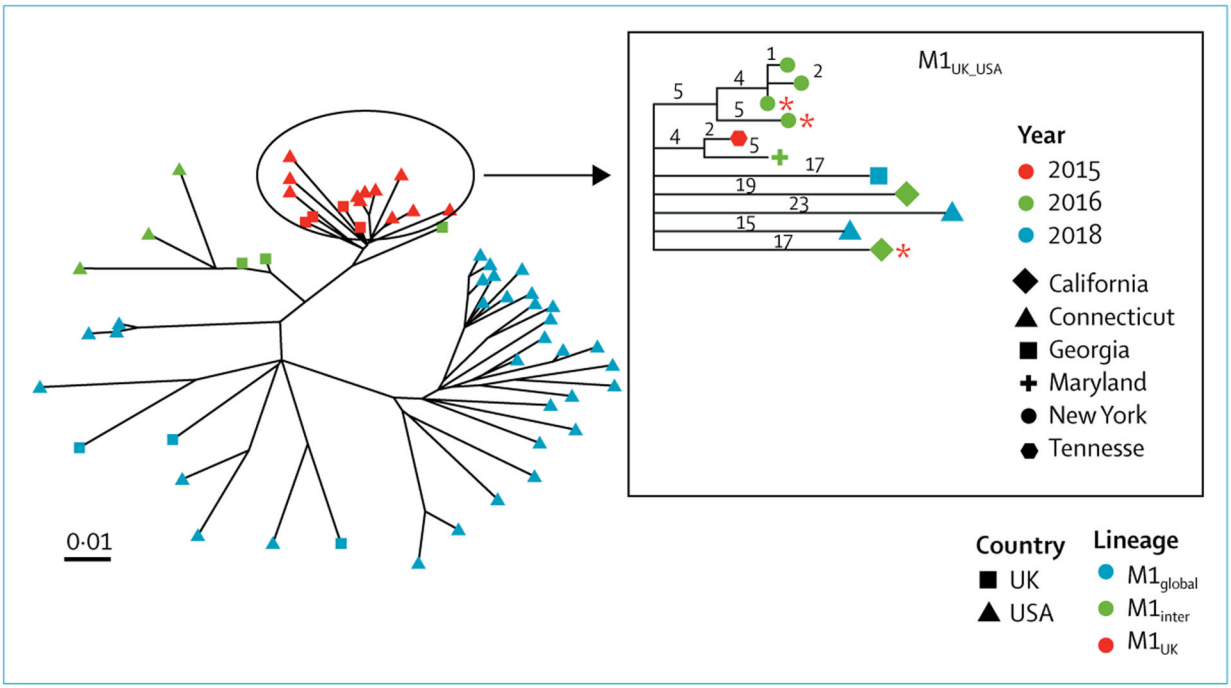

Figure: Phylogenetic relationship of the UK and USA isolates belonging to the $M1_{UK}$ lineage

A maximum likelihood phylogenetic tree was constructed from core SNPs (excluding those potentially acquired by horizontal gene transfer) of *emm*1 group A streptococcus isolates, including the 11 $M1_{UK\_USA}$ isolates, six $M1_{inter\_USA}$ isolates identified in our whole-genome sequencing analysis ($M1_{inter}$ isolates have been reported previously;[1] $M1_{inter\_USA}$ isolates contained eight to 13 of the 27 lineage-defining SNPs of $M1_{UK}$), and 29 randomly selected $M1_{global\_USA}$ isolates (held in the Active Bacterial Core surveillance system) from the USA, as well as four randomly selected $M1_{UK}$ isolates, three randomly selected $M1_{inter}$ isolates, and three randomly selected $M1_{global}$ isolates from the UK.[1] Shading highlights the $M1_{UK}$ lineage. The scale bar represents the expected nucleotide substitutions per site. The inset shows the genetic relatedness of the 11 $M1_{UK\_USA}$ isolates. Branch length is dictated by SNP difference. SNP=single-nucleotide polymorphism. *Fatal cases.