Published in final edited form as:
Pediatr Infect Dis J. 2015 December ; 34(12): 1414–1415. doi:10.1097/INF.0000000000000878.

Molecular Epidemiology of Group A Streptococcus Infections in Cambodian Children, 2007 - 2012

Paul Turner, MB BS, PhD, FRCPCH, FRCPath[1,2,*], **Pises Ngeth, MD**[3], **Claudia Turner, MB BS, PhD, FRCPCH**[1,2], **Sena Sao**[3], **Nicholas P.J. Day, MD, FRCP**[2,4], **Ciara Baker, MSc**[5], **Andrew C. Steer, MB BS, PhD, FRACP**[5,6,†], and **Pierre R. Smeesters, MD, PhD**[5,6,†]

[1]Cambodia-Oxford Medical Research Unit, Angkor Hospital for Children, Siem Reap, Cambodia [2]Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, UK [3]Angkor Hospital for Children, Siem Reap, Cambodia [4]Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand [5]Group A Streptococcal Research Group, Murdoch Childrens Research Institute, Melbourne, Australia [6]Centre for International Child Health, University of Melbourne, Melbourne, Australia

Keywords

Group A Streptococcus; emm-type; vaccine; children; epidemiology

To The Editors

Group A *Streptococcus* (GAS) is responsible for significant morbidity and mortality globally. Two strong vaccine candidates are currently under evaluation: a 30-valent type-specific M protein-based vaccine and a vaccine targeting the conserved J8 region of M protein.[1] The 30-valent vaccine covers the most frequent serotypes circulating in high-income countries but coverage may be sub-optimal in low-income settings with greater GAS *emm* type diversity.[2] Sixty eight allelic variants have been described for J8 and the relationship between allelic diversity and vaccine efficacy is unclear.[1] Limited epidemiologic data are available from many regions making vaccine coverage estimates imprecise: there are no previous data for low-income countries in South East Asia.[2]

The clinical microbiology database at Angkor Hospital for Children, a non-governmental pediatric hospital serving the population of northern Cambodia, was searched to identify clinical GAS isolates cultured between 1st January 2007 and 31st December 2012. These isolates underwent molecular *emm*-typing: *emm*-clusters, and the J8 vaccine antigen content, were deduced from the *emm*-typing result as previously described.[3] 30-valent vaccine

[*]**Corresponding author:** Dr Paul Turner; Cambodia-Oxford Medical Research Unit, Microbiology Department, Angkor Hospital for Children, PO Box 50, Siem Reap, Cambodia; pault@tropmedres.ac; Telephone: +855 89287059.
[†]These senior authors contributed equally to this article

Conflicts of Interest: The authors have no conflicts of interest to declare.

Note: These data were presented in part at the XIX Lancefield International Symposium on Streptococci and Streptococcal Diseases, Buenos Aires, Argentina

Europe PMC Funders Author Manuscripts

coverage was estimated using currently available cross-opsonization data.[3, 4] Strain diversity was assessed by Simpson's Reciprocal Index.

One hundred fifty GAS isolates from 149 patients were characterized. The median patient age was 3.8 years (range 0 – 18.6). 118 (78.6%) isolates were from skin and soft tissue infections, 16 (10.7%) from bloodstream infections, 7 (4.7%) from bone/joint infections, 7 (4.7%) from pharyngitis, and 2 (1.3%) from infections at other sites. 50 *emm*-types were identified from 13 *emm*-clusters and two isolates were considered non-typeable (see Supplemental Digital Content, Table). No novel *emm*-types were identified. The Simpson Reciprocal Index was 28.5 (95% confidence interval (CI) 23.1 – 37.3) indicating considerable diversity, similar to that seen in other low income countries.[2]

Potential coverage of the J8 vaccine was predicted to be excellent with 43 (28.7%) and 104 (69.3%) isolates predicted to have the J8 and J8.1 allele, respectively. Therefore, J8 vaccine coverage could be expected to be 98.0% (95% CI 94.2 – 99.6%). Fifty isolates (33.3%) were of *emm*-types covered by the 30-valent vaccine and an additional 42 isolates (28.0%) have been shown to be potentially covered by the vaccine as a result of cross-opsonization. Therefore, the potential coverage could be expected to be 61.3% (95% CI 53.0 – 69.2%) but may be higher since 26.0% of the isolates belong to 16 *emm*-types which have not yet been examined for evidence of cross-opsonization.

Comparison with the only other available regional dataset, revealed considerably greater *emm*-type diversity in the Cambodian isolates compared with those isolated in Thailand between 1985-2004.[5] Fifty nine *emm*-types from 13 *emm*-clusters were represented in the combined dataset. Only eight of the 13 *emm*-clusters were found in Thailand. There were 10 shared *emm*-types, comprising 64.2% of the Thailand isolates but only 26.4% of the Cambodia isolates.

Our study had several limitations. Pharyngeal isolates were not well represented due to clinician sampling practices and also there was an absence of adult sampling in the dataset. Also, the population studied may not be representative of Cambodia as a whole. Finally, comparisons between the current data and the Thailand dataset are limited by the differences between the study populations and non-overlapping study periods.

Overall, these data indicate a high diversity of circulating GAS strains in Cambodia, the potential high coverage of the J8 vaccine candidate and the need for complementary studies to assess the potential coverage of the 30-valent vaccine candidate. These results highlight the need for robust regional and country-level data for vaccine planning purposes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of Funding: CT, PT, and NPJD are supported by the Wellcome Trust of Great Britain.

Europe PMC Funders Author Manuscripts

References

1. Moreland NJ, Waddington CS, Williamson DA, et al. Working towards a group A streptococcal vaccine: report of a collaborative Trans-Tasman workshop. Vaccine. 2014; 32:3713–3720. [PubMed: 24837510]
2. Steer AC, Law I, Matatolu L, Beall BW, Carapetis JR. Global *emm* type distribution of group A streptococci: systematic review and implications for vaccine development. Lancet Infect Dis. 2009; 9:611–616. [PubMed: 19778763]
3. Sanderson-Smith M, De Oliveira DM, Guglielmini J, et al. A systematic and functional classification of *Streptococcus pyogenes* that serves as a new tool for molecular typing and vaccine development. J Infect Dis. 2014; 210:1325–1338. [PubMed: 24799598]
4. Dale JB, Penfound TA, Chiang EY, Walton WJ. New 30-valent M protein-based vaccine evokes cross-opsonic antibodies against non-vaccine serotypes of group A streptococci. Vaccine. 2011; 29:8175–8178. [PubMed: 21920403]
5. Yoonim N, Olive C, Pruksachatkunakorn C, Good MF, Pruksakorn S. M protein typing of Thai group A streptococcal isolates by PCR-Restriction fragment length polymorphism analysis. BMC Microbiol. 2005; 5:63. [PubMed: 16225702]