WHO/FCH/CAH/05.07

The Current Evidence for the Burden of Group A Streptococcal Diseases

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Acknowledgements

WHO/CAH wishes to thank Prof. Jonathan R Carapetis, Centre for International Child Health, University of Melbourne Department of Paediatrics, Royal Children's Hospital, Melbourne, Australia for undertaking this review, and Dr. Andrew C Steer and Prof. E. Kim Mulholland, Royal Children's Hospital, Melbourne, Australia, for contributing to it. WHO/CAH is grateful to Drs. Alan Bisno, Singh Chhatwal, Hala Hamsa, Ed Kaplan, Fran Rubin, and Anne Schuchat for reviewing the draft manuscript and providing valuable comments..

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List of abbreviations

ACTH	Adreno-corticotrophic hormone
APSGN	Acute post-streptococcal glomerulonephritis
ARF	Acute rheumatic fever
CMR	Crude mortality rate
GAS	Group A streptococcus
IE	Infective endocarditis
RHD	Rheumatic heart disease
SES	Socio-economic status
SMR	Standardised mortality rate
UN	United Nations
WHO	World Health Organization

Executive summary

Group A streptococcus (GAS) causes a broad spectrum of disease, from severe invasive infections and the post-streptococcal complications of acute rheumatic fever (ARF) and acute post-streptococcal glomerulonephritis (APSGN) to mild superficial infections of the throat or skin. These diseases may lead to further complications (e.g. ARF may cause rheumatic heart disease, which in turn may be further complicated by endocarditis or strokes).

The only GAS disease for which global disease burden estimates have previously been made is rheumatic heart disease (RHD). Systematic reviews were conducted to ind all published and unpublished data relating to the burden of each manifestation of GAS disease. We aimed to include only recent data, and population-based data where possible, and applied incidence and prevalence estimates to population denominator data from the UN Population website. We defined the following regions according to presumed homogeneity of GAS disease rates: Sub-Saharan Africa, South-Central Asia, People's Republic of China, other countries in Asia (excluding Japan), Latin America, Middle East and North Africa, Eastern Europe, Pacific Island countries and indigenous Australian and New Zealand, and Established Market Economies.

RESULTS

Burden of Disease

We conclude that approximately 18.1 million people currently suffer from a serious GAS disease, another 1.78 million new cases occur each year, and these diseases are responsible for over 500,000 deaths each year (See table below). Added to this are over 111 million prevalent cases of streptococcal pyoderma, and 616 million new cases of GAS pharyngitis each year.

Summary of estimated global burden of group A streptococcal diseases

Disease	Number of existing cases	Number of new cases each year	Number of deaths each year
Rheumatic heart disease	15.6 million	282,000*	233,000**
History of acute rheumatic fever without carditis, requiring secondary prophylaxis	1.88 million	188,000*	
RHD-related infective endocarditis		34,000	8,000
RHD-related stroke	640,000	144,000	108,000
Acute post-streptococcal glomerulonephritis	-	472,000	5,000
Invasive group A streptococcal diseases		663,000	163,000
Total severe cases	**18.1 million**	**1.78 million**	**517,000**
Pyoderma	111 million		
Pharyngitis		616 million	

All estimates rounded off. Note that these estimates assume constancy of incidence and prevalence over time.

* New RHD cases were calculated based on the proportion of incident ARF cases expected to develop RHD. The remainder of incident ARF cases are included in the "History of ARF without carditis" row. Therefore, the total number of new ARF cases each year is 282,000 + 188,000 = 470,000.

** Includes ARF deaths. RHD deaths are based on proportion of existing RHD cases expected to die each year.

\- No attempt has been made to quantify the prevalence of APSGN-induced chronic renal impairment or end-stage renal failure

The vast majority of all of these cases came from less developed countries (79% of RHD cases, 95% of ARF cases, 97% of APSGN cases, 97% of invasive GAS cases). We have used relatively conservative assumptions at each step, so these are minimum summary estimates of the burden of GAS diseases.

Quality of data

There were many areas where the data were deficient, particularly from less developed countries. We found sufficient data to be confident of the estimates for prevalence of RHD, and for incidence of invasive GAS diseases in more developed countries. All of the remaining estimates (ARF incidence, APSGN incidence, ARF/RHD mortality, invasive GAS disease incidence in less developed countries, RHD-related IE and stroke, pyoderma prevalence, GAS pharyngitis incidence) are based on relatively poor-quality data, particularly in some regions. Therefore, there is considerable uncertainty surrounding the estimates presented here. However, at each step we have attempted to make assumptions that tend to under-estimate rather than over-estimate the burden of disease. The estimates presented here relate to numbers of cases and deaths. GAS causes disease predominantly in children and young adults, so the burden to communities in terms of years of potential life lost is even higher than reflected purely in terms of numbers of cases and deaths.

CONCLUSIONS

Even given the limitations of the data on which they are based, these estimates suggest that GAS causes a substantial burden of disease and death on a global scale, mainly in children and young adults and in less developed countries (although they also remain relatively important diseases in more developed countries).

The data presented here also indicate that GAS diseases are highly prevalent in some regions, but may be less so in others. For example, RHD is very common in Sub-Saharan Africa and the Pacific, common in South-Central Asia and the Middle East / North Africa, but apparently less common in many Asian countries and Latin America. The ARF incidence data do not always match the RHD prevalence data. In some cases, this may be due to reducing incidence of ARF, which precedes by some years a reduction in RHD prevalence. However, a more likely explanation is the poor quality of data from some regions, particularly Sub-Saharan Africa, Asia and South-Central Asia. The pyoderma data also suggest regional differences in prevalence, which cannot be solely attributed to climate or socio-economic conditions. For example the highest pyoderma prevalences were documented in the Pacific region, whereas poorer, tropical African countries had substantially lower prevalences. The data were inadequate to draw any conclusions regarding regional differences regarding ARF/RHD mortality, APSGN, invasive GAS disease, or pharyngitis. Better data from a number of key regional sites in less developed countries would allow a more detailed analysis of regional differences and perhaps reveal markers that might enable local authorities to determine if they should be investing resources into efforts to control GAS diseases. Such data may also improve our understanding of the individual diseases and how to prevent them.

PRIORITY ISSUES

The burden of GAS diseases and the association of these diseases with poverty cannot be ignored. It is now critical to develop mechanisms for data collection to provide disease burden estimates with greater confidence. Regional variations in disease burden and the paucity of data relating to particular diseases and outcomes make it critical to improve data collection in less developed countries.

Field sites are needed for intensive population based GAS disease burden studies (including bacteraemia surveillance) in less developed countries. Ideally, at least one site would be established in each of Sub-Saharan

Africa, Pacific Island nations, East or South-east Asia, and South-Central Asia. In many regions there are already instutions with the necessary infrastructure, and even some with baseline GAS epidemiological data (e.g. the Wellcome/KEMRI Clinical Research Unit in Kenya, where bacteraemia data are being collected), which would simplify the process of establishing GAS field sites. There are a number of research institutes in South-Central Asia that collect GAS epidemiological data; it should not be difficult for one site to expand its program to collect information on all GAS diseases, or perhaps for a collaborative project to be established across institutes.

In addition to collecting complete epidemiological data, these sites could attempt to develop simpler tools for making some GAS disease burden estimates in other less developed countries. These field sites would also likely be ideal locations for future clinical trials of GAS vaccines, with the aim of evaluating their efficacy against the GAS diseases of greatest importance to less developed countries.