



VacZine Analytics

Bringing life to vaccine strategy..

DiseaseINFOPACK

Group A *Streptococcus*: invasive disease

July 2008

Abstract

DiseaseINFOPACK: *Group A Streptococcus (invasive disease)*

CAT No: VADIP006, published July 2008

REPORT ABSTRACT:

Group A Streptococcus (GAS) is a Gram-positive organism commonly found in the throat and skin. Although colonization with GAS is mostly harmless, the bacteria can cause a wide spectrum of diseases and inflammatory sequelae. GAS infections range from mild superficial infections such as pharyngitis “strep throat” to severe invasive life-threatening diseases such as necrotizing fasciitis (NF) or “flesh eating disease”. GAS is also responsible for rheumatic heart disease which is estimated to kill 200-300,000 people each year (WHO figures).

This **DiseaseINFOPACK** report is an expert review of the current literature with a focus on invasive diseases. An emphasis is placed on GAS molecular pathogenesis, clinical outcomes coupled with methods of prevention and control. A review of US and EU epidemiology is also provided including analysis of US ABC surveillance and StrepEURO data.

PAGES: 49

Table of contents

Executive Summary

Author's Note

The Pathogen

GAS: classification of diseases

GAS: classification of diseases (cont..)

Types of GAS species

Transmission of GAS

Pathogenesis

Pathogenesis (cont..)

Proteins involved in GAS pathogenesis

Focus on M-protein

Host response to GAS

iGAS disease – Overview

iGAS disease – three overlapping syndromes

Focus on necrotizing fasciitis (NF)

Clinical outcome/pathology

Focus on Streptococcal Toxic Shock Syndrome (STSS)

Case definition for STSS

Focus on bacteremic GAS pneumonia

Risk factors for iGAS infection

Risk groups for iGAS infection

Prevention and Control

Treatment of iGAS disease

Overall morbidity/mortality

iGAS syndromes: review of mortality estimates

Epidemiology – surveillance

Epidemiology – highlights

Epidemiology – focus on US

Epidemiology – focus on EU

Epidemiology – StrepEURO update 2008

Epidemiology – key trends and dynamics

iGAS – economic impact

iGAS – summary of key issues

iGAS – opportunity for new strategies

Appendices I/II

Bibliography


1. US Centers for Disease Control and Prevention. Group A Streptococcal Disease. Available at: http://www.cdc.gov/ncidod/dbmd/diseaseinfo/Groupastreptococcal_g.htm. Accessed May 2008.
2. Martin JM., et al. Group A Streptococcus. *Semin Pediatr Infect Dis* 17: 140-148.
3. **Adapted from:** The World Health Organisation (WHO). A Review of the technical Basis for the Control of the Conditions Associated with Group A Streptococcal Infections. Available at: Accessed May 2008.
4. Widdowson., JP et al. An M-associated protein antigen (MAP) of group A streptococci. *J Hyg (Lon)* 1971; 69:553-64.
5. Carapetis JR., et al. The epidemiology and prevention of Group A Streptococcal infections: acute respiratory tract infections, skin infections and their sequelae at the close of the 20th Century. *Clin Infect Dis* 1999; 28: 205-11.
6. Hamburger M., et al. Studies on the transmission of hemolytic Streptococcus infections. I: Cross infection in army hospital wards. *J. Infect. Dis.* 75, 58-70.
7. Factor SH., et al. Invasive Group A Streptococcal disease: risk factors for adults. *Emerg Infect Dis.* 2003; 9:970-7.
8. Srisikandan S., et al. *Streptococcus pyogenes*. Insight into the function of the Streptococcal superantigens. *Int J Biochem & Cell Biol* 2007: 39; 12-19.
9. Cunningham MW., et al. Pathogenesis of Group A Streptococcal infections. *Clin. Microbial. Rev.*, 13, 470-511.
10. Bohach GA., et al. Staphylococcal and Streptococcal pyrogenic toxins involved in toxic shock syndrome and related illnesses. *Crit. Rev. Microbial.* 1990: 17; 251-272.
11. Faulkner L., et al. The mechanism of superantigen-mediated toxic shock: Not a simple Th1 cytokine storm. *J. Immunol.* 2005: 175; 6870-6877.
12. Stevens DL., et al. Severe Group A Streptococcal infections associated with a toxic-shock like syndrome and scarlet fever toxin A. *N. Engl. J. Med.* 1989: 321; 1-7.
13. Sharma S., et al. Streptococcus Group A Infections. eMedicine from WebMD. Available at: <http://www.emedicine.com/med/TOPIC2184.HTM>. Accessed May 2008.
14. Lancefield RC. Current knowledge of the type specific M antigens of Group A Streptococci. *J Immunol* 1962; 89: 307-313.
15. Johnson DR. et al. Epidemiologic analysis of Group A Streptococcal serotypes associated with severe system infections, rheumatic fever, or uncomplicated pharyngitis. *J infect Dis* 1992; 166: 374-382.
16. Lancefield RC. The antigenic complex of *Streptococcus hemolyticus*. I. Demonstration of type specific substance in extracts of *Streptococcus hemolyticus*. *J Exp Med* 1928; 47:91-103.
17. Kotb M., et al. An immunogenetic and molecular basis for differences in outcomes of invasive Group A Streptococcal infections. *Nature Medicine* (2002) 8, 1398 – 1404.
18. O'Brien KL., et al. Epidemiology of invasive group A Streptococcus disease in the United States, 1995-1999. *Clin Infect Dis* 2002; 35:268-76.
19. US Centers For Disease Control and Prevention (CDC). Active Bacterial Core Surveillance Reports, Emerging Infections Program Network, Group A Streptococcus. Available at: <http://www.cdc.gov/ncidid/dbmd/abcs/survreports.htm>.
20. **Adapted from:** Wessels MR. Group A Streptococcal disease in the 1990s: New clues to pathogenesis. *Int J Infect Dis* 1996; 1: 107-114.
21. Bisno AL., et al Streptococcal infections of skin and soft tissues. *N Eng J Med* 1996: 334: 240-245.
22. Maynor MM. Necrotizing Fasciitis. *The Medscape Journal, emedicine.* Available at: <http://www.emedicine.com/EMERG/topic332.htm>. Accessed July 2008.
23. **Adapted from:** Committee on Infectious Diseases. Severe invasive Group A Streptococcus infections: a subject review. *Pediatrics* 101: 136-140, 1998.
24. Muller PM., Clinical and epidemiological features of Group A Streptococcal Pneumonia in Ontario, Canada. *Arch Intern Med* 2003: 163; 467-472.
25. O'Loughlin RE, et al. The epidemiology of invasive Group A Streptococcal infection and potential vaccine implications: United States, 2000-2004. *Clin Infect Dis.* 2007;45:853-62.
26. US Centers For Disease Control and Prevention. Morbidity and Mortality Weekly (MMWR) 2003: 52 (06); 106-109.
27. US Centers For Disease Control and Prevention. Morbidity and Mortality Weekly (MMWR) 1997: 46(40); 944-948.
28. Greene CM., et al. Cluster of deaths from Group A Streptococcus in a long-term care facility, Georgia, 2001. *Am J Infect Control* 2005: 33: 108-13.
29. Prevention of Invasive Group A Streptococcal Infections Workshop Participants. *Clin Infect Dis* 2002; 35:950-9 (erratum: *Clin Infect Dis* 2004; 39: 325-32).

Bibliography (cont..)

31. Lamagni TL et al. The epidemiology of severe *Streptococcus pyogenes* associated disease in Europe. *Eurosurveillance* 2005; Vol. 10. Issues 7-9.
32. Carapetis RC., et al. The global burden of Group A Streptococcal diseases. *Lancet Infect Dis* 2005; 5: 685-694.
33. Schwartz B., et al. Group A Streptococcal outbreaks in nursing homes. *Infect Control Hosp Epidemiol* 1992; 13:742-7.
34. Centers for Disease Control and Prevention. 2003. Active Bacterial Core Surveillance (ABCs) report. Group A Streptococcus, 2006. Available at: <http://www.cdc.gov/ncidod/dbmd/abcs/survreports/gas06.pdf>. Accessed May 2008.
35. Working Group on Prevention of Invasive Group A Streptococcal Infections. Prevention of invasive group A streptococcal disease among household contacts of case-patients: is prophylaxis warranted? *JAMA*. 1998;279:1206-1210.
36. Feely EA. Necrotizing Fasciitis. Diagnostic Modalities. Available at: http://intmedweb.wfubmc.edu/grand_rounds/1998/necrotizing_fasciitis.html#Treatment. Accessed July 2008.
37. Loughlin RE., et al. The epidemiology of Invasive Group A Streptococcal Infection and Potential Vaccine Implications. *Clin Infect Dis*. 2007; 45:853-62.
38. Hribalova V. *Streptococcus pyogenes* and the toxic shock syndrome. *Ann Intern Med*. 1988; 108 (5) 772.
39. Strep-EURO. Main website. Available at: http://www.strep-euro.lu.se/about_ver2.html. Accessed: July 2000.
40. Jasir A., et al. Epidemiology of severe *S.pyogenes* infections in Europe (STREP-EURO PROJECT). Session talk presented at XVII Lancefield International Symposium on Streptococci and Streptococcal Diseases, 22-26 June, 2008. Porto Heli, Greece.
41. Cone LA. Clinical and bacteriologic observation of a toxic shock-like syndrome due to *Streptococcus pyogenes*. *N Eng J Med*. 1987; 317:146-14.
42. Institute of Medicine. In: Stratton KR, ed. *Vaccines for the 21st Century*. Washington , DC: National Academy Press, 2001: 181-8.
43. Widjaja, AB. The hospital costs of treating necrotizing fasciitis (NF). *ANZ. J.Surg*. 2005. 75; 1059-1064(6).
44. Factor SH., et al. Risk factors of Pediatric Invasive Group A Streptococcal Disease. *Emerg Infect Dis*. 2005; 11(7).

About VacZine Analytics:

VacZine Analytics is a brand new research consultancy based in the United Kingdom. Its aim is to provide high quality-disease and commercial analysis to those working within or in collaboration with the vaccine industry.

-  With our product lines:
 - DiseaseINFOPACK
 - OpportunitySCAN
 - MarketVIEW
 - ExpertREACT
 - VaccineSTATS

Our key focus is helping clients to build the case for developing new vaccines.

Disclaimer

All rights reserved

This licensed product (or part thereof) may not be reproduced, stored in a retrieval system or transmitted in any form without the written permission of the publisher VacZine Analytics (a division of Assay Advantage Ltd).

The facts presented within this document, at the time of its production, were believed to be correct and were gathered in good faith from both primary and secondary sources. VacZine Analytics is not always in the position to assure that the facts are guaranteed. VacZine Analytics cannot be held liable for any actions based upon facts or recommendations presented within this document.



VacZine Analytics

Bringing life to vaccine strategy...

www.vacZine-analytics.com

Warren House

Bells Hill

Bishops Stortford

Herts

CM23 2NN

United Kingdom

Tel. +44 (0) 1279 654514

e-mail: info@vacZine-analytics.com

© VacZine Analytics, 2008. All rights reserved.