Proceedings of the Ninth International Pathogenic Neisseria Conference

The Guildhall, Winchester, England
September 26th-30th 1994

Compiled and edited by
Janet S. Evans, Susan E. Yost,
Martin C.J. Maiden and
Ian M. Feavers
THE NINTH INTERNATIONAL PATHOGENIC NEISSERIA CONFERENCE

Meeting Coordinators
Dr. Martin C.J. Maiden, Division of Bacteriology, National Institute for Biological Standards and Control, Potters Bar, UK
Dr. Ian M. Feavers, Division of Bacteriology, National Institute for Biological Standards and Control, Potters Bar, UK

Scientific Committee and Meeting Secretariat
Dr. M. Achtman, Max-Planck-Institut für molekulare Genetic, Berlin, Germany
Dr. M.J. Corbel, Division of Bacteriology, National Institute for Biological Standards and Control, Potters Bar, UK
Dr. I.M. Feavers, Division of Bacteriology, National Institute for Biological Standards and Control, Potters Bar, UK
Dr. E. Griffiths, Division of Bacteriology, National Institute for Biological Standards and Control, Potters Bar, UK
Dr. J. Heckels, University of Southampton, UK
Dr. R. Demarco de Hormaeche, University of Cambridge, UK
Dr. D.M. Jones, OBE, Public Health Laboratory, Manchester, UK
Dr. M.C.J. Maiden, Division of Bacteriology, National Institute for Biological Standards and Control, Potters Bar, UK
Professor H. Smith, CBE, FRS, University of Birmingham, UK
Professor B. Spratt, FRS, University of Sussex, UK
Dr. M. Virji, University of Oxford, UK
Dr. W. Zollinger, Walter Reed Army Institute for Research, Washington, USA

Meeting Sponsors
Biocine S.p.A
Glaxo Group Research Limited
Lederle-Praxis
Mérieux UK Limited
National Institute for Biological Standards and Control, UK
North American Vaccine Inc
SmithKline Beecham Pharmaceuticals
Unipath Limited
United Kingdom Department of Health
Wellcome Trust
World Health Organisation
Zeneca Pharmaceuticals
Preface

Over the years a number of different approaches have been taken for the publication of the proceedings of the International Pathogenic *Neisseria* Conferences, including invited articles in journal supplements and the production of commercial books based on 'camera-ready' material supplied by delegates at the conference. During the preparation for the Ninth Conference there was much discussion as to the relative virtues of a number of previously used and novel approaches. Finally, we decided to attempt a new format, that of an extended abstract book that is available to the delegates during the conference itself. We felt that the greatest value of a book of the meeting is as a 'snapshot' view of the current status of *Neisseria* research, and therefore placed most emphasis on speed of production. Judging by the number and length of the articles, this approach has been popular with the delegates and we hope that the book proves to be useful. We also plan to publish a separate delegate directory, which will be available to delegates at the meeting.

By taking advantage of the widespread availability of word-processing software we asked delegates wishing to present their work at the meeting to send an extended abstract on computer diskette three months before the date of the meeting. This was the last possible date that enabled us sufficient time to compile the book and hopefully most of the work described in the following pages is still current. Our main task has been to compile the articles sent to us and to typeset them in a uniform format. We have also done a limited amount of editing, mainly to correct typographical errors and, very occasionally, to improve the clarity of the text.

This book aims to fulfill two roles, an abstract book for use at the conference itself and a reference book to cover the period up to the next conference. The book is therefore organised into the same subject headings as the conference sessions and these are presented in the same order as they will occur in the Scientific Programme. Under each heading, the oral presentations are given first followed by the poster presentations. For the posters, the poster number is given at the top of the article: as all of the posters will be on display for the whole meeting they have numbered consecutively from 1 (the first poster in 'Capsules and lipopolysaccharides' to 185 (the last poster in 'Vaccines and vaccine trials').
# Table of Contents

**Capsules and lipopolysaccharides** ................................................. 1

Chemically modified *Neisseria meningitidis* capsules as vaccines  
H.J. Jennings ................................................................. 3

Molecular basis and biological significance of encapsulation and capsule modification  
in meningococci  
M. Frosch ................................................................. 5

Genetic and functional analysis of the lipopolysaccharide of *Neisseria gonorrhoeae*  
B.D. Robertson, E.T. Schwan, H. Brade and J.P.M. van Putten. .................... 7

Isolation of mutants of *Neisseria meningitidis* producing altered LPS  
P. van der Ley, H.J. Hamstra, M. Kramer, L. Steeghs, A. Petrov and J.T. Poolman . 8

The biology of the lipooligosaccharides of the pathogenic *Neisseria*  
M. A. Apicella, D. Zhou, F. Lee, M. Ketterer, N. Porat, M. Blake, B. Gibson and  
D. Stephens ................................................................. 10

Structural relationships and sialylation among meningococcal lipooligosaccharide  
(LOS) serotypes  
J. McL. Griffiss, B. Brandt, J. Engstrom, H. Schneider, W. Zollinger, B. Gibson ... 12

The structure of lipooligosaccharide produced by *Neisseria gonorrhoeae*, strain  
15253 isolated from a patient with disseminated infection: Evidence for a new  
glycosylation pathway of the gonococcal lipooligosaccharide  

Surface charge and hydrophobicity correlate with Gc behaviour  
J. Swanson ................................................................. 16

Molecular analysis of mAb 2C7 and mAb CA1, an anti-idiotpe surrogate for a  
conserved gonococcal oligosaccharide epitope  
S. Gulati, W. Den, S. Sompuram, J. Sharon, D.P. McQuillen and P.A. Rice ...... 19

Functional characteristics of the immune response to the gonococcal  
lipooligosaccharide epitope defined by mAb 2C7 in natural infection and after  
immunization  
D.P. McQuillen, S. Gulati, E.W. Hook and P.A. Rice ............................... 21

Cloning and sequencing of lipooligosaccharide monoclonal antibody regions for  
molecular level study of epitope-antibody interactions  
J.S. Evans and M.C.J. Maiden ............................................. 23

Application of FPLC to purification of lipooligosaccharide from meningococcal  
strains  
J.S. Evans and M.C.J. Maiden ............................................. 26
Isolation of an S. typhimurium rfaE homolog in Neisseria gonorrhoeae
F.K. Lee and M.A. Apicella ........................................ 28

Lipooligosaccharide biosynthesis in Neisseria gonorrhoeae: Cloning, identification
and characterization of the "1,5 heptosyltransferase I gene (hepTI)
D. Zhou and M.A. Apicella ........................................ 29

Genetic analysis of a locus for gonococcal LOS biosynthesis
E.C. Gotschlich .................................................. 30

Regulation of phase variation of gonococcal lipooligosaccharide expression
R.J. Danaher, J. Levin, D. Arking, R. Sandlin and D.C. Stein ................. 32

Influence of lipooligosaccharide structure on the sensitivity of serogroup B Neisseria
meningitidis to normal human serum
C.M. Kahler and D.S. Stephens ..................................... 34

Influence of capsular polysaccharide and LOS sialylation on serum resistance and
invasive properties in meningococci serogroups A, B and C
S. Hammerschmidt, A. Unkmeir, J.P.M. van Putten and M. Frosch ........... 36

Effects of capsule and lipooligosaccharide sialylation on the serum resistance of
Neisseria meningitidis
F.G. Mackinnon, R. Borrow, A.J. Fox, A. Robinson and D.M. Jones ........ 38

Phenotypic switching of LOS immunotype expression during murine infection with
Neisseria meningitidis
F.G. Mackinnon and A. Robinson .................................... 41

The relationship between encapsulation and sialylation of meningococcal
lipooligosaccharide
R. Borrow, A.J. Fox and D.M. Jones .................................. 43

Biology of major surface proteins .................................. 47

Neisseria porin proteins
John E. Heckels ................................................... 49

Measurement of antibodies to variable regions of meningococcal class 1 outer
membrane proteins using ELISA with synthetic peptides as coating antigens
E.M. Rouppe van der Voort, C.C.A.M. Peeters, P. Hoogerhout, L.M. Bouter and
J.T. Poolman .................................................. 51

Comparison of human and murine monoclonal IgGs specific for the P1.7
meningococcal porin
Michaelsen and M. Achtman ....................................... 52

Serum opsonins induced during the course of meningococcal disease correlate with
anti-outer membrane protein antibodies
H-K. Guttormsen, L.M. Wetzler and C.O. Solberg ........................................ 54

Regulation of protein 1 porin (P1) function by host cell factors and biological implications of P1 insertion into target cell membranes
T. Rudel, D. Lorenzen, I. Heuer, R. Benz, R. Kolb and T.F. Meyer .................. 57

Pili and Opc in meningococcal virulence: phenotypic requirements and molecular mechanisms
M. Virji ........................................................................................................... 58

Identification of pilin domains of Neisseria meningitidis involved in eucaryotic cell interactions
M. Marceau, J-L Beretti and X. Nassif ......................................................... 61

Function of PilC as the pilus adhesin and the interaction of PilC with host cells and other neisserial factors
T. Rudel, I. Scheuerpflug, A.F. Kahrs, J. Maier and T.F. Meyer .................... 63

The gonococcal PilT protein plays an essential role in pilus-associated phenotypes of twitching motility and natural competence for transformation
M. Koomey, R. Fox, L. Brossay and J. Hebert ............................................. 64

The structure and assembly of N. gonorrhoeae pilin
K. Forest, H. Parge, M. Hickey and J. Tainer .................................................. 66

Biology of the Opc protein from Neisseria meningitidis

Genetics and function of Opa proteins: progress and unanswered questions
J.G. Cannon ..................................................................................................... 70

Genetic regulation by non-homologous recombination in N. gonorrhoeae
R.J. Belland and S.G. Morrison ....................................................................... 73

Several of the gonococcal Opa proteins share a common epitope and functional features with host cell proteins such as LOS binding and 4B12 reactivity: Evidence for heterophile bidectional adherence and host cell activation
M.S. Blake, N. Porat, H. Qi and M.A. Apicella .............................................. 74

Pili and Opa are required for HEC-1-B cell microvillus elongation and engulfment of Neisseria gonorrhoeae
J.M. Griffiss, C.J. Lammel, S. Zhao, J. Wang, N.P. Dekker and G.F. Brooks .... 76

Identification of human linear B-cell epitopes on the class 1 and 3 outer membrane proteins of Neisseria meningitidis using synthetic peptides
Immunisation with liposomes containing recombinant meningococcal class 1 protein generates bactericidal, subtype specific antibody
S.J.Ward, D.A.White, I.N.Clarke and J.E.Heckels ........................ 80

Immunisation with synthetic peptides containing epitopes of the class 1 outer-membrane protein of Neisseria meningitidis: Production of bactericidal antibodies on immunisation with cyclic and multiple antigen peptides
M. Christodoulides and J.E. Heckels .................................. 82

Humoral immune responses to different forms of a meningococcal class 1 outer membrane protein
Hoogerhout and J.T. Poolman ...................................... 84

Cloning and expression of porA, the gene encoding the class 1 outer membrane protein from Neisseria meningitidis: Purification and immunological characterization of the recombinant polypeptide
and L. Herrera ................................................. 85

The P1.10 subtype as a model for structural and immunological studies of meningococcal typing reagents
J. Suker, S. Yost, M.C.J.Maiden and I.M. Feavers ........................ 87

Measurement of antibodies to variable regions of meningococcal class 1 outer membrane proteins using ELISA with synthetic peptides as coating antigens
E.M. Rouppe van der Voort, C.C.A.M. Peeters, P. Hoogerhout, L.M. Bouter and
J.T. Poolman .................................................. 89

Porin peptide ELISA for the serologic diagnosis of disseminated gonococcal infection

Transcriptional regulation of the class 1 outer membrane protein in group B
Neisseria meningitidis
J. Farley, A. Masi, B. Novitsky and R. Hazelo ............................... 92

Phase variation of class 1 outer membrane protein in Neisseria meningitidis by transcription from a variable promoter region
vander Ende .................................................. 94

Irreversible phase variation of class 1 outer membrane protein by deletion of the complete porA gene
A. van der Ende, C.Th.P. Hopman and J. Dankert ........................... 95

Construction and analysis of meningococcal mutants for the P64k antigen
A. Martín, M. Delgado, G. Véliz, A. Musacchio, R. Silva, G. Guillén and L. Herrera
.................................................................................. 96
Monoclonal antibodies specific to a 64 kDa protein from *Neisseria meningitidis*
C. Nazábal, S. Cruz, T. Carmenate, A. Musacchio, R. Silva, M. Delgado,
S. González, G. Guillén and L. Herrera ................................ 98

Microevolution of the *opc* gene: Recombinational variants of two uralleles
A. Seiler, R. Reinhardt, J. Sarkari and M. Achtman ....................... 100

Cloning and expression of *opc*, the gene encoding the outer membrane protein 5C
from *Neisseria meningitidis*: Purification and immunological characterization of the
recombinant polypeptide
T. Carmenate, A. Alvarez, S. González, A. Musacchio, O. Niebla, M. Delgado, R.
Silva and G. Guillén ............................................ 101

*Neisseria gonorrhoeae* Opa protein function: Structure-activity studies
D.J.J. Simon, J.T. Liu, M.S. Blake, C.M Blake and R.F. Rest ................ 103

Transformation and expression of Opa proteins in *Neisseria gonorrhoeae*
S. Hill .......................................................... 106

Under construction: *Escherichia coli* encoding multiple gonococcal factors as a
model for studying *Neisseria gonorrhoeae* salpingitis
G.L. Gorby, A.F. Ehrhardt, M.A. Apicella, C. Elkins, R.F. Rest and D. Simon ... 107

Immunodetection of the *mtr* associated outer membrane protein in *Neisseria
gonorrhoeae*
R.M Delahay, C.A Ison and M.J Gill .................................... 110

Regulation of recombination and DNA repair in *Neisseria gonorrhoeae*
C.G. Black, J.A.M. Fyfe and J.K. Davies .............................. 112

The repertoire of silent pilin gene copies and their chromosomal location is similar
but not identical in gonococcal strains FA1090 and MS11
T.L. Snodgrass, J.A.F. Dempsey and J.G. Cannon .......................... 113

Generation of a novel pilin locus using CAT fusions in *Neisseria gonorrhoeae*
B. S. Howell, L. A. Wainwright and H. S. Seifert ........................ 116

Cloning and sequence analysis of a *pilR/pilS* homologue from *Neisseria
gonorrhoeae*
C.S. Carrick, J.A.M. Fyfe and J.K. Davies .............................. 118

Site-directed mutagenesis of the promoter region of the gonococcal *pilE* gene
J.A.M. Fyfe, C.S. Carrick and J.K. Davies .............................. 119

Characterization of Gene Products Involved in Gonoccocal Pilus Biogenesis
N. E. Freitag and M. Koomey ........................................ 120

The product of the *pilQ* gene is essential for the biogenesis of type IV pili in
*Neisseria gonorrhoeae*
S. L. Drake and J. M. Koomey ........................................... 122
Characterization of *omc*, gene required for type IV pili biogenesis and competence in *Neisseria gonorrhoeae*

S.L. Drake and J.M. Koomey .................................................. 124

The *plsC* Gene of *Neisseria meningitidis* and *Neisseria gonorrhoeae*

J.S. Swartley, J. Balthazar, J. Coleman, W.M. Shafer and D.S. Stephens ........ 125

Pilus-mediated attachment of *Neisseria gonorrhoeae* and *Neisseria meningitidis* to host cell receptors

M. Rahman, S. Normark and A-B. Jonsson .................................. 127

Modulation of pilus-facilitated adherence of *Neisseria meningitidis* by pilin primary sequence changes, post-translational modification and PilC expression


Anti-Gal binds to pilus of *Neisseria meningitidis*: the IgA isotype blocks complement-mediated killing

R. M. Hamadeh, G. A. Jarvis, M. Estabrook and J. McL. Griffiss ............. 132

**Environmentally regulated proteins and metabolism** .......................... 135

Transferrin-binding proteins of *Neisseria meningitidis*


Purification of *Neisseria meningitidis* transferrin binding proteins and characterisation by epitope mapping and iron release studies

A.R. Gorringe, L.I. Irons, P. Aisen, O. Zak and A. Robinson ................ 140

Characterization of the gonococcal transferrin receptor

C. Nau Cornelissen, J.E. Anderson, M. Kashkari, J. Watson and P.F. Sparling ... 143

Iron-acquisition and disease produced by pathogenic *Neisseria*

H.C. Wiesenfeld, A.J. Nowalk, B.J. Wahlberg, P. Adhikari, and T.A. Mietzner ... 144

*Neisseria* Cytotoxins


Regulation of *aniA* expression by oxygen availability in *Neisseria gonorrhoeae* and *N. meningitidis*

V.L. Clark and L.E. Silver .................................................. 148

Electron microscopic localisation of iron-regulated proteins in *N. meningitidis* with particular reference to the lactoferrin and transferrin receptors

N.B.L. Powell, D.A.A. Ala'aldeen, A.B. Schryvers and S.P. Borriello .......... 150

Genetic heterogeneity of gonococcal transferrin-binding proteins

J.E. Anderson, J.R. Watson, R.J. Kim, P.F. Sparling and C.N. Cornelissen .... 151
Production of meningococcal transferrin binding protein 2 in \textit{E.coli}
M. Legrain, D. Speck, R. Brandely, D. Schubnel, M.-J. Quentin-Millet and E. Jacobs ................................................................. 152

Development and optimization of a gene replacement system for the \textit{tbp} genes of \textit{N. meningitidis}
S.D. Gray-Owen, L. Wang, G.C. Gonzalez, and A.B. Schryvers, ............ 153

Characterization of a highly structured domain in Tbp2 from \textit{N. meningitidis}
involved in the binding to human transferrin
R.A. Vonder Haar, M. Legrain, A. Findeli, H.V.J. Kolbe and E. Jacobs .... 156

Identification of transferrin binding regions of the \textit{Neisseria meningitidis} transferrin receptor proteins by the use of chimeric Tbp's
S.W. Irwin, C. A. Fuller and A.B. Schryvers ................................. 157

Identification of the domains of human transferrin involved in binding to transferrin receptors of human pathogens by the use of chimeric recombinant transferrins expressed in a baculovirus expression system
A. Kabani, L. Button and A. B. Schryvers ..................................... 159

Transferrin-transferrin receptor interactions in \textit{Neisseria meningitidis}
N.D. Sharma, A. Bomford, R.W. Evans, B. Gorinsky, P. Stevenson and E. Griffiths ................................................................. 161

Antigenicity and cross-reactivity of purified \textit{Neisseria meningitidis} transferrin binding protein 2 (TBP2)
C. Ferreirós, M.T. Criado, L. Ferrón and M. Pintor ......................... 162

Human and animal immune response to meningococcal transferrin-binding proteins: implications for vaccine design

Blocking of iron uptake from transferrin by antibodies against the transferrin-binding system of \textit{Neisseria meningitidis}
C. Ferreirós, M.T. Criado, L. Ferrón and M. Pintor .......................... 166

Production of monoclonal antibodies to meningococcal transferrin binding protein 2
S. Fourage, P. Dumas, L. Lissolo, M. Mignon, M.J. Quentin-Millet and C. Hurpin 168

Mapping monoclonal antibodies directed against meningococcal transferrin-binding protein 2

Identification of the protective component within the meningococcal transferrin-binding protein complex
L. Lissolo, G. Maitre-Wilmotte, P. Dumas, M. Mignon, B. Danve and M.-J. Quentin-Millet ...................................................... 170
Biochemical and genetic analysis of the lactoferrin binding protein and lbpA gene of Neisseria spp.
R.A. Bonnah, R.-H. Yu and A. B. Schryvers ........................................ 171

Cloning a lactoferrin (Lf) receptor gene from Neisseria gonorrhoeae and characterization of strains unable to use Lf-bound iron
G.D. Biswas and P.F. Sparling ......................................................... 173

Characterization of FrpB, the 74kD iron-regulated, outer-membrane protein of N. gonorrhoeae
M. Beucher and P.F. Sparling ......................................................... 174

Cloning and DNA sequence of the gene coding for a DnaK homologue from Neisseria meningitidis
A. Martín, T. Menéndez, S. González, E. Caballero, A. Musacchio, R. Silva and G. Guillén ............................................................. 175

Homology models of N. gonorrhoeae ferric binding protein
M.A. McTigue, A.S. Arvai, T.A. Mietzner and D.E. McRee .......................... 177

High affinity iron-binding by Fbp is homologous to the transferrins at both the structural and functional level
A.J. Nowalk and T.A. Mietzner ......................................................... 178

Heavy metal inhibition of pathogenic Neisseria
R.E. Michael, K.L. Veraldi and T.A. Mietzner .................................... 180

Promoter mapping and transcriptional regulation of the iron-regulated Neisseria gonorrhoeae Fbp gene
C.R. Ekechukwu, S. Subbarao, P.J. Desai, S.A. Morse and C.A. Genco ........... 182

Use of operon fusions to study the effect of gonococcal Fur on iron-regulated gonococcal genes
S. Subbarao and S.A. Morse .............................................................. 184

Isolation of a Neisseria gonorrhoeae fur mutant and its analysis by 2-D protein gel electrophoresis
C.E. Thomas and P.F. Sparling .......................................................... 187

Analysis of the complexity of iron regulation by Neisseria gonorrhoeae
R.C. Nzeribe and C.A. Genco ........................................................... 189

Characterization of haemin transport in Neisseria gonorrhoeae
P.J. Desai, M. I. Torres, R.C. Nzeribe and C.A. Genco ................................ 191

Identification of an iron-regulated outer membrane protein of Neisseria meningitidis involved in the utilization of haemoglobin complexed to haptoglobin
L.A. Lewis and D.W. Dyer ................................................................. 193

Lactoferrin and haemoglobin iron-utilization does not influence the transmission of
Neisseria gonorrhoeae
H.C. Wiesenfeld, H.D. Bittner, R.L. Sweet and T.A. Mietzner ................. 194

Identification and characterization of a gene in Neisseria meningitidis and Neisseria gonorrhoeae that enables an Escherichia coli TonB mutant to grow with ferrichrome A as the sole iron source
S.A. Berish and S.A. Morse ...................................... 196

Environmentally-regulated, periplasmically-located [Cu, Zn]-superoxide dismutase from N. meningitidis: Another virulence factor?
K.E. Wilks, P.R. Langford and J.S. Kroll ........................................ 199

Environmental control of gonococcal sialyltransferase activity, LOS biosynthesis, sialylation and sensitivity to serum killing
R. Rest, D. Bell, J. Ferguson, J. Liu, D. McGee and R. Talukdar .................. 200

Novel gene organization for carA and carB in Neisseria gonorrhoeae
F.S. Lawson and J.R. Dillon ........................................ 202

Cloning and sequencing of the meningococcal polyphosphate kinase gene: Production of mutants in polyphosphate synthesis
C.R. Tinsley and E.C. Gotschlich ........................................... 204

Novel lipoprotein found in meningococci
Q-L. Yang, C.R. Tinsley and E.C. Gotschlich .................................. 206

Characterization of the Phosphoglucone isomerases of Neisseria gonorrhoeae and Neisseria meningitidis
T. Tønjum, D.A. Caugant, E. Namork and M. Koomey ......................... 208

44,000 dalton proteins of Neisseria gonorrhoeae
R.C. Judd .......................................................... 210

Genetic characterization of the str and sucAB-lpd operons of Neisseria gonorrhoeae
S.F. Porcella, R. Belland and R.C. Judd ........................................ 212

Genetics of gonococcal resistance to toxic hydrophobic antimicrobial agents
K.E. Hagman, W. Pan, B.G. Spratt, R.C. Judd and W.M. Shafer ................. 213

The effects of co-incubation of Lactobacillus acidophilus on Neisseria gonorrhoeae catalase activity
H-y Zheng, T.M. Alcorn and M.S. Cohen ........................................ 216

Use of antibiotics to select auxotrophic mutants of Neisseria meningitidis
A.L. Erwin, M.J. Gill and E.C. Gotschlich ..................................... 217

Identification and characterization of auxotrophs of Neisseria meningitidis produced by Tn916 mutagenesis
A.L. Erwin and D.S. Stephens ............................................... 219
Host-pathogen interactions ................................................................. 221

In vivo experiments with Neisseria gonorrhoeae
Myron S. Cohen, Susan Isbey, Larry Charniga, Ann Jerse, Leesa Whicker, H. Steven Seifert and Janne G. Cannon ........................................... 223

Association of gonococcal lipooligosaccharide phenotype with virulence
H. Schneider, R.A. Kuschner, J.W. Boslego, A.S. Cross and C.D. Deal .... 225

Studies on gonococcal pilin antigenic variation

A low Mr moiety released from blood cell fractions which enhances CMP-NANA sialylation of LPS in gonococci
N.J. Parsons, C. Constantinidou, J.A. Cole and H. Smith ........................ 229

Dynamics of the interaction between gonococci and epithelial cells
J.P.M. van Putten, S.M. Paul, B.D. Robertson and E.T. Schwan ............... 230

Immunogenicity and evolutionary variability of IgA1 protease from Neisseria meningitidis

Structure and biological function of the components of the IgA protease polyprotein precursor

Clinical aspects of Neisseria meningitidis infections
P. Brandtzaeg .................................................................... 234

Enhanced immune response to meningococcal antigens in C5 deficient mice
J. Andreoni and P. Densen .......................................................... 236

Phagocytosis of Neisseria meningitidis in complement deficient individuals depends on the C3 deposition onto its surface and the IgG receptor (Fc (R) allotypes of the granulocytes

Effect of Gc LOS sialylation on antibody deposition and complement activation
T. Zaleski and P. Densen .......................................................... 241

Neisseria meningitidis isolates from terminal complement component deficient and complement sufficient individuals
A. Orren, D.A. Caugant, C.A.P. Fijen, E.J. van Schalkwyk and G.J. Coetzee ... 243

Immune responses to meningococcal outer membrane antigens induced by
tonsillopharyngeal carriage of *Neisseria meningitidis*
E. Rosenqvist, E. Wedege, E.A. Høiby, D.A. Caugant, G. Bjune and L.O. Frøholm ........................................................... 245

The use of murine-human heterohybridomas to produce gonococcal specific human isotype antibodies
M.D. Cooper, G.A. Jarvis and R. Kirkpatrick .......................... 247

Relationship of the onset of symptoms and dysuria to opacity protein (protein II) expression in experimental gonorrhea

Specific unresponsiveness to LPS during infections by *Neisseria gonorrhoeae*
R. Demarco de Hormaeche, L.M. Chamberlain and C.E. Hormaeche ........... 250

Immune responses to capsular polysaccharides of *Neisseria meningitidis* in two C2-deficient sisters: Role of the alternative pathway in serum bactericidal reactions
B. Selander, A.G. Sjöholm, E. Holmström, L. Truedsson, H. Käyhty, E. Wedege and C. Söderström ................................................ 253

Susceptibility to meningococcal disease: Association with rare complement C7 variants?
G. Dewald, C. A.P Fijen, E. J. Kuijper and J. Dankert ..................... 255

Serum factors affecting the sensitivity to *Neisseria meningitidis* lipopolysaccharide
A.B.Petrov, J.A.Hazelzet, L. Aarden and J.T. Poolman .................... 257

Molecular and genetic analysis of an adhesion- and invasion-deficient *Neisseria meningitidis* serogroup B mutant
E.M. Ribot, N.J. Raymond, K.A. Birkness, D.S. Stephens and F.D. Quinn .... 258

The influence of capsule and LPS phenotype on the invasion potential of a serogroup B strain expressing Opc and pili
M. Virji, I. Peak, K. Makepeace, M. Jennings, D.J.P. Ferguson and E.R. Moxon .. 260

Meningococcal outer-membrane protein Opc mediates interactions with multiple extracellular matrix components
M. Virji, K. Makepeace and E.R. Moxon ................................ 263

Interactions of *Neisseria meningitidis* expressing Opc and Opa proteins with human phagocytes
G. McNeil, M. Virji and E.R. Moxon ....................................... 265

Opc interactions at the apical surface of polarised endothelial cells require serum factors that bind to the integrin family of cell surface receptors
M. Virji, K. Makepeace and E. R. Moxon .................................. 268

Investigations into the molecular basis of meningococcal toxicity for human endothelial cells: the role of LPS and pili

xvii
Quantitative analysis of the interaction of Neisseria meningitidis with human nasal epithelium *in vitro*

Inhibitory effects of saliva on binding of meningococci to epithelial cells

Virus infection and meningococcal disease

Exposure to cigarette smoke and colonization by Neisseria species

Are monocytes the “Trojan horses” of meningococcal disease?

Neisserial porins induce upregulation of B cell co-stimulatory ligand, B7-2: Possible mechanism behind their adjuvant activity
L.M. Wetzler

Neisserial porins inhibit human neutrophil actin polymerization, degranulation, opsonin receptor expression and phagocytosis, but prime neutrophils to increase their oxidative burst

The effects of pro- and anti-inflammatory cytokines on the neutrophil oxidative burst response to pathogenic and nonpathogenic strains of Neisseria meningitidis
P. Kragsbjerg and H. Fredlund

The pattern of early neutrophil and platelet activation in an *ex-vivo* model of meningococcal bacteraemia
N.J. Klein, R.S. Heyderman, C.A. Ison, M. Peakman and M. Levin

Assessment of candidate anti-inflammatory treatments in an *in vitro* whole blood model of meningococcal sepsis
B. Chan, P. Kalabalikis, N. Klein, R. Heyderman and M. Levin

Passage of Neisseria meningitidis through a tissue culture bilayer mode
K.A. Birkness, B.L. Swisher, E.G. Long, E.H. White, E.P. Ewing, Jr. and F.D. Quinn

Erythrocytal latex agglutination test and its modification
A.A. Demina and Yu.V. Martynov
Population biology and epidemiology .............................. 303

The population biology of the pathogenic Neisseria
B.G. Spratt, G. Carpenter, E. Feil, M. O'Rourke, N.H. Smith and J. Zhou ....... 305

Analysis of chromosomes from Neisseria meningitidis strains

Molecular methods in the determination of the relationships between meningococcal population biology and epidemiology
M.C.J. Maiden, J. Suker, I.M. Feavers, and J.A. Bygraves ................. 309

Analysis of Neisseria meningitidis class 3 outer membrane protein gene variable
regions and type identification using genetic techniques
M.C. Bash, K.B. Lesiak, S.D. Banks, and C.E. Frasch ..................... 312

Molecular analyses of meningococcal serosotyping antibodies
I.M. Feavers, S.E. Yost, and M.C.J. Maiden .......................... 314

Use of PCR for detection and typing of tetM determinant in Neisseria
gonorrhoeae
C.A. Ison, N. Tekki, C. Phanis, P.J. Woodford, and M.J. Gill .............. 317

Patterns of PCR-RFLP of Neisseria meningitidis group B and their epidemiologic
significance
Zhu Peixuan and Hu Xujing ........................................ 319

Detection of bacterial DNA in cerebrospinal fluid with a simultaneous assay for
Neisseria meningitidis, Haemophilus influenzae and Streptococci by a seminested
PCR strategy
P. Olcén, A. Bäckman, N. Qian, P. Kragsbjerg, C. Påhlson and P. Rådström .... 321

Continued spread of meningococcal disease caused by serogroup A Neisseria
strains isolated in France (1987-1994)
J.Y. Riou, E.A. Höiby, M. Guibourdenche, F. Varaine, G. Sperber, K. Rahal, M.
Wouafo, J.P. Lombart, P. Fagot, C. Joguet and D.A. Caugant ......... 322

Epidemiology of Neisseria meningitidis - impact of new techniques
D.M. Jones ........................................................ 324

Enhanced epidemiological surveillance for meningococcal disease by DNA-based
sub-typing of meningococci
A.J. Fox, D.M. Jones, E. Sutcliffe, M.C.J. Maiden and I.M. Feavers ....... 327

Identification of epidemiologically important meningococcal genotypes by Restriction
Fragment Length Polymorphism analysis
S.J. Gray, A.J. Fox and D.M. Jones .................................. 329
Neisseria meningitidis
R. Urwin, A.J. Fox, D.M. Jones, I.M. Feavers and M.C.J. Maiden ............ 331

Monoclonal antibody to serotype 17 of Neisseria meningitidis and their prevalence in Brazilian states
C.T.Sacchi, A.P.S.Lemos, M.C.O.Gorla, C.E.A.Melles and C.E.Frasch ........ 334

Ribotyping as an additional molecular marker of Neisseria meningitidis Serogroup C epidemic strains

A PCR assay for differentiating two groups of 25.2 Mda TetM Neisseria plasmids
M.C. Roberts, Y. Pang and M. Xia ........................................ 335

PCR AREA Differentiates between strains of Neisseria meningitidis
B.-E. Kristiansen, C. Fermer and O. Sköld ................................ 337

An approach to study the molecular genetics of Neisseria meningitidis: Partial sequence of rpoB gene and genetic variability
O.Nolte ................................................................. 338

Characterization of Neisseria meningitidis by polymerase chain reaction and restriction endonuclease digestion of the M-6 gene
R. Silva, L.M. Alonso, M. de Jesús Leal, A. Martin, G. Guillén and L. Herrera ... 339

PCR for diagnosis of meningococcal meningitis: its application to the cerebrospinal fluids collected during the Norwegian serogroup B vaccine protection trials

DNA sequence analysis of antigenic diversity in Neisseria meningitidis class 3 outer membrane proteins
R. Dalseg, E. Wedege and D. A. Caugant .................................... 343

Rapid diagnosis of meningococcal meningitis by the polymerase chain reaction
Z. Peixuan and H. Xujing .................................................. 345

Comparative evaluation of suspicious meningococcal cases with nPCR and ELISA
N.B. Saunders, D.R. Shoemaker, B.L. Brandt and W.D. Zollinger .............. 346

Importance of the use of subtype P1.9 monoclonal antibody for the serotyping of Neisseria meningitidis Serogroup B strains in Brazil
E.N. De Gaspari, A.A. Ribeiro Filho, C.N. Baccoccine and W.D. Zollinger .... 348

The physical map of a Group A strain of Neisseria meningitidis shows a region of complex DNA rearrangement relative to the chromosomes of Neisseria gonorrhoeae strains FA1090 and MS11
J.F. Dempsey and J.G. Cannon ............................................ 349

Pulsed field gel electrophoresis analysis of the ET-37 complex of Neisseria meningitidis

xx
Clonal analysis of Neisseria meningitidis serogroup B serotype 15 strains of Germany using pulsed-field gel electrophoresis
I. Ehrhard, F.-B. Spencker and H.-G. Sonntag ........................................ 354

Analysis of meningococci from a New Zealand hyperendemic using serotyping, subtyping and restriction fragment length polymorphism typing
S.J. Walker, R.J. Whyte, Y.M. Galloway and D.R. Martin .......................... 355

Genomic fingerprinting of meningococcal group C ET-15 disease isolates by pulsed field gel electrophoresis
F.E. Ashton, A. Ryan, L. Mancino, F. Collins and W. Johnson .................. 358

Emergence of a new virulent clone within the ET-5 complex of serogroup B meningococci in Norway
E. Wedege, J. Kolberg, A. Delvig, E.A. Hoiby, E. Holten, E. Rosenqvist and D.A. Caugant ................................................ 361

Meningococcal disease in Europe: Concerted action on all aspects of disease management
W. Thiel, A.J. Fox and participants in the EMGM .................................. 363

Factors affecting meningococcal carriage and acquisition in military recruits

Dynamic characteristics of the meningococcal carrier state
J. Andersen and I. Lind. ................................................................. 366

Phenotypic and genotypic characterization of Neisseria meningitidis isolates from carriers in households with infants
I. Lind, L. Berthelsen and S.F. Olsen ................................................. 368

The epidemiological cycle of meningococcal infection in Russia (1969-1993)
Yu.V. Martynov and A.A. Demina ....................................................... 370

Neisseria meningitidis and bacterial meningitis in Moscow
I.S. Korolyova and T.V. Ilyina ............................................................. 372

Clinical course of meningococcal disease in one district of the Czech Republic
L. Roznovsky, J. Matuska, P. Kriz, J. Smykal, E. Kostricova and J. Wiedermann ................................................................. 374

Characterization of nontypeable and nonsubtypeable Neisseria meningitidis strains isolated in the Czech Republic
M. Musilek, P. Kriz, V. Danielova and J. Holubova ................................ 375

New epidemiological situation in the Czech Republic due to Neisseria meningitidis C:2a:P1.2 (P1.5) ........................................................................ 375
Significance of bactericidal antibodies directed against capsular and noncapsular antigens of \textit{Neisseria meningitidis}

P. Kris and B. Kris

Serotypes and subtypes of \textit{Neisseria meningitidis} strains isolated in Moscow during the decrease of morbidity (1989-1991)

N.N. Kostyukova, M.Ch.Gorlina, T.F. Chernysheva, A.I.Mishina, T.I. Skirda and H. Kaythy

Serum bactericidal activity in a secondary school population following an outbreak of meningococcal disease


Meningococcal disease in Romania 1971-1992

F. Mihalcu, O. Pasolescu, I. Levenet and A. Iacob

Characteristics of meningococcal isolates from patients and carriers in the Balkans

D.A. Caugant, J. Kremastinou, G. Tzanakaki, F. Mihalcu, L.E. Smart and C.C. Blackwell

Group C meningococcal disease in São Paulo, Brazil: a reemerging pathogen


Group B meningococcal disease in São Paulo, Brazil: An epidemiological and microbiological study


Mathematical modelling of age-specific incidence of meningococcal disease

A.E.Platonov, V.B. Beloborodov and L.V.Kulagina

Probabilistic spatial-temporal model as a simulator for the epidemiology of directly transmitted infections: Updated version for meningococcal infection

A.E.Platonov and L.V.Kulagina

Meningococcal disease as a problem of the special intensive care unit for patients with infectious diseases

V. Beloborodov, A. Platonov and D. Troshansky

Single-dose ofloxacin to eradicate tonsillopharyngeal carriage of \textit{Neisseria meningitidis}

O.H. Gilja, A. Halstensen, A. Digranes, H. Mylvaganam, A. Aksnes and E.A. Høiby

Antibiotic prescribing and meningococcal disease

Identification of amino acid residues crucial for sulfonamide resistance in the chromosomal *dhps* gene in *Neisseria meningitidis* by site-directed mutagenesis
C. Fermér, B.-E. Kristiansen, O. Sköld and G. Swedberg .......................... 405

Changes in the resistance to ampicillin and tetracycline of *Neisseria gonorrhoeae* isolated in Stockholm 1982-1993
M. Bäckman, K. Jacobson and S. Ringertz ........................................ 406

Variable sequences between the *carA* and *carB* genes of pathogenic and commensal *Neisseria* species
F.S. Lawson, F.M. Billowes and J.R. Dillon ...................................... 408

Relationship of source of health care and antimicrobial susceptibility patterns of *Neisseria gonorrhoeae*
K. K. Winterscheid, W. L. Whittington, J. Hale and K.K. Holmes .................. 409

Epidemiologic analysis of *Neisseria gonorrhoeae* by pulsed-field gel electrophoresis
M. Xia, W. L. Whittington, J. S. Knapp, K. K. Holmes and M. C. Roberts .......... 411

Gonorrhoea surveillance among female commercial sex workers from Mexico City
C. J. Conde-Glez, F. Uribe, A. Cruz, M. Hernández and E. Calderón ................ 413

A comparison of three methods for the culture confirmation of *Neisseria gonorrhoeae* strains currently circulating in the UK
K.R. Gough, A.E. Jephcott and A. Turner ........................................... 416

Comparative typing of gonococci using pyrolysis mass spectrometry: Preliminary experiments
J.T. Magee, K.R. Gough, J. Yang and A. Turner ..................................... 418

Genetic diversity of *por* for differentiating between isolates of *Neisseria gonorrhoeae*
C.A. Ison and N. Anwar ................................................................. 420

**Vaccines and vaccine trials** ......................................................... 423

The development of new meningococcal vaccines
R. Rappuoli, A. Gianozzi, S. D’Ascenzi, C. Ceccarini, A. Bartaloni and P. Costantino 425

Immunization of juvenile rhesus monkeys with group B *Neisseria meningitidis* capsular polysaccharide-protein conjugate vaccines

Development of conjugate vaccines against *Neisseria meningitidis*
Joseph Y. Tai, Francis Michon and Peter C. Fusco ................................. 430

Development of a multivalent class 1 OMP containing meningococcal vaccine
J. Poolman ................................................................. 431
A vaccine against group B meningococci composed of the outer membrane protein P1 produced in *Bacillus subtilis* and renatured *in vitro*
P. H. Mäkelä, S. Butcher, I. Idänpään-Heikkilä, M. Nurminen, S. Muttilainen, K. Runeberg-Nyman, M. Sarvas and E. Wahlström ...................... 432

Phase I and phase II clinical studies of group A serotype 4 protein vaccine in infants in China

Quality control of the Cuban and Norwegian serogroup B vaccines used in the Iceland study
E. Griffiths, G. Sierra and J. Holst ........................................... 437

Immunogenicity of two outer membrane protein-based serogroup B meningococcal vaccines among young adults in Iceland

Antibody response of complement deficient patients to tetravalent meningococcal polysaccharide vaccine
C.A.P. Fijen, E.J. Kuijper, Y. van Leeuwen, M.R. Daha and J. Dankert ........ 440

Bactericidal antibody responses of juvenile rhesus monkeys to *Neisseria meningitidis* conjugate B polysaccharide vaccines

Serological analyses from preclinical studies on meningococcal conjugate vaccines
P.C. Fusco, P.D. Lohmar, R.M. Msays, F. Michon and J.Y. Tai ................. 443

Vaccination of mice with outer membrane protein detoxified LPS complexes mainly induces antibodies that do not recognize intact outer membrane vesicles
E.N. De Gaspari and W.D. Zollinger ........................................... 444

Safety and immunogenicity of meningococcal lipopolysaccharide incorporated into liposomes for monkeys

The use of meningococcal detoxified lipooligosaccharide in experimental vaccines against group B meningococci

Role of IgM antibodies against C polysaccharide in the bactericidal antibody titres of Brazilian vaccinees
L.G. Milagres, C.E.A. Melles, S.E. Maslanka and G.M. Carlone ................. 447
Immune response of mice to a Brazilian group B meningococci vaccine
L.G. Milagres, M.C.C. Brandleone, C.T. Sacchi, V.S.D. Vieira, R.C. Zanella,
M.C. Gorla, A.P.S. Lemos and C.E. Frasch ........................... 448

Phase I study of two meningococcal outer membrane protein vaccines prepared
from a class 4 outer membrane protein negative mutant and its isogenic parent
and J. Mays................................................. 449

Immune response to outer membrane vesicle vaccines of LPS mutants of the
vaccine strain 44/76 of Neisseria meningitidis
S. R. Andersen, G. Bjune, K. Bryn and E. Jantzen ........................ 451

Human antibody kinetics to meningococcal outer membrane antigens after
vaccination with the Norwegian group B outer membrane vesicle vaccine: Results
from a pilot three-dose trial among Norwegian adults
E.A. Høiby, E. Rosenqvist, E. Wedege, G. Bjune and H. Nakleby ............. 453

A retrospective cohort study of the possible association between demyelinating
diseases and immunization with the Norwegian MenB outer membrane vesicle
vaccine
P. Aavitsland, G. Bjune and J. Fuglesang .................................. 455

Comparison of the class 1 outer membrane protein from B: 15:P1.16 Neisseria
meningitidis strains isolated from patients previously immunised with a serogroup B
outer membrane protein vaccine in Norway
J.L. Brooks, E. Rosenqvist, G. Bjune, P.R. Lambden, and J.E Heckels ........ 457

Antibody response against the 64 kDa protein from Neisseria meningitidis after
systemic meningococcal disease, and after vaccination with two different serogroup
B meningococcal vaccines among young adults in Iceland
A. Musacchio, S. González, E. Caballero, E.A. Høiby and E. Rosenqvist .... 460

Cross-reactive bactericidal components in sera from the serogroup B meningococcal
vaccine trial in Iceland

Immunoblot analyses of vaccination sera from the serogroup B meningococcal
vaccine trial in Iceland
E. Wedege, E.A. Høiby, G.M. Carlone and E. Rosenqvist .................... 464

Opsonic activity against meningococci in vaccination sera from the serogroup B
meningococcal vaccine trial in Iceland
T.E.Michaelsen, A.Aase, A.K.Pedersen, G.M.Carlone, E.A.Høiby and
E.Rosenqvist ................................................ 466

Reactogenicity of two outer membrane protein-based serogroup B meningococcal
vaccines among young adults in Reykjavik, Iceland
H. Briem, K. Jónsdóttir and B. A. Perkins ................................. 468
Comparison of serum bactericidal results using vaccine type-strains and heterologous target strains to evaluate immunogenicity of two meningococcal serogroup B vaccines in Iceland
G.M. Carlone, D. Williams, J. Dykes, D. Kapczynski, B.D. Plikaytis and B.A. Perkins ................................................................. 470

Quality control of a serum bactericidal assay and other laboratory protocols used in a Neisseria meningitidis group B vaccine immunogenicity study in Iceland

Assessment of the vaccination with meningococcal polysaccharide vaccine in two localities of the Czech Republic
P. Kriz, J. Vlčkova, A. Galetkova and M. Bobak ......................................................... 475

The Neisseria meningitidis outer membrane protein P1 produced in Bacillus subtilis and reconstituted into phospholipid vesicles elicits antibodies to native P1 epitopes
S. Muttilainen, I. Idänpää-Heikkilä, E. Wahlström, M. Nurminen, P.H. Mäkelä and M. Sarvas ............................................................. 477

The antibody response to a prototype liposome vaccine containing Neisseria meningitidis outer membrane protein P1 produced in Bacillus subtilis
I. Idänpää-Heikkilä, S. Muttilainen, E. Wahlström, L. Saarinen, M. Sarvas and P.H. Mäkelä ................................................................. 479

Use of a parenteral component priming - oral immunization regimen to elicit protection against Neisseria gonorrhoeae in vivo

A possible influence of vaccine induced Por, LOS, and Rmp antibodies on the outcome of intraurethral challenge with Neisseria gonorrhoeae
P.A. Rice, E.W. Hook, M.S. Blake, R.S. Kaslow, S. Gulati, P.K. Kohl, M. VanRadden and T.M. Buchanan .............................................. 483

Protective effect elicited by vaccination with a live, attenuated strain of Neisseria gonorrhoeae
L.M. Chamberlain, R. Demarco de Hormaeche and C.E. Hormaeche ........................ 485