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ANALYSIS OF THE GENETIC DIVERSITY OF *NEISSERIA MENINGITIDIS* IN SOUTH AFRICA

GARRY BRIAN COULSON

2005

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DECLARATION

The experimental work described in this dissertation was conducted under the supervision of Dr. Anthony Smith and Dr. Anne von Gottberg (Respiratory and Meningeal Pathogens Research Unit) National Institute for Communicable Diseases, National Health Laboratory Service, Johannesburg, South Africa.

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I declare that this dissertation is my own unaided work. It is being submitted for the Degree of Master of Science in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

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ABSTRACT

Meningococcal disease is an important cause of morbidity and mortality worldwide, particularly in children and young adults. Epidemics caused by *Neisseria meningitidis* continue to plague many countries on a global scale, none more so than countries of the African 'meningitis belt', where attack rates can reach up to 1000/100,000 population. It has been well recognized that most epidemic and endemic cases of meningococcal disease are caused by a limited number of genetically defined clonal groups. The objective of this molecular epidemiological study was to genotypically characterize strains of *N. meningitidis* collected in South Africa from July 1999 to July 2002. Characterization of meningococcal strains belonging to serogroup A, B, C, W135 and Y, by PFGE and MLST allowed us to determine the genetic population structure of *N. meningitidis* in South Africa, and thus identify the predominant clonal groups responsible for the majority of meningococcal disease in the country over this period. The results from the genotypic characterization revealed that the greatest majority of meningococcal disease in South Africa was caused by a strains belonging to only a few "hyperinvasive lineages", most notably strains of the ST-44 complex (lineage III), ST-32 complex (ET-5 complex), ST-11 complex (ET-37 complex), and the ST-1 complex (subgroup I/II) which have all been responsible for major epidemics worldwide. These findings have direct implications on public health decision, particularly with regards to the development of effective intervention and control strategies, and emphasize the need for continuous long-term monitoring of the circulation of these strains in the population.

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This dissertation is dedicated to Mom and Dad, who knew just the right combination of kind words of encouragement and a kick in the rear to get me through to the end.

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PUBLICATION

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PRESENTATION

Coulson GB, Whitney A, Klugman K and Popovic T. Genotypic Characterization of *Neisseria meningitidis* in the U.S. and South Africa. 14th International Neisseria Pathogenic Conference, September 5-10, 2004. Milwaukee, Wisconsin USA.

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LIST OF ABBREVIATIONS

>	Greater than
<	Less than
%	Percentage
°C	Degrees Celsius
ml	Millliliter
min	Minute
µl	Microliter
µM	Micromolar
secs	Seconds
et al.	And others
i.e.	That is
bp	Base pair
hrs	Hours
ATP	Adenosine triphosphate
CO_2	Carbon dioxide
CSF	Cerebrospinal fluid
CTAB	Cetyltrimethylammonium bromide
DNA	Deoxyribonucleic acid
dNTP	Deoxynucleoside triphosphate
EDTA	Ethylenediaminetetraacetic acid
ET	Electropherotypes
LPS	Lipopolysaccharide
$MgCl_2$	Magnesium chloride
MLEE	Multi-locus enzyme electrophoresis
MLST	Multi-locus sequence typing
mM	Millimolar
NHLS	National Health Laboratory Service
NICD	National Institute for Communicable Diseases
OMP	Outer membrane protein

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PCR	Polymerase chain reaction
PFGE	Pulsed-field gel electrophoresis
RAPD	Random amplified polymorphic DNA
RFLP	Restriction fragment length polymorphism
rpm	Revolutions per minute
SDS	Sodium dodecyl sulphate
SS-PCR	Serogroup-specific PCR
ST	Sequence type
TAE	Tris-acetate-EDTA
TBE	Tris-borate-EDTA
TE	Tris-EDTA
USA	United States of America
WHO	World Health Organization

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