

Mycology Reference Unit

BACKGROUND

The Mycology Reference Unit (MRU) aims to contribute to the control of fungi of public health and clinical importance by undertaking relevant, laboratory-based surveillance and research projects, and functioning as a reference laboratory in the field of clinical mycology.

ACTIVITIES, HIGHLIGHTS AND ACHIEVEMENTS

THE GERMS-SA CRYPTOCOCCAL SURVEILLANCE PROJECT

The cryptococcal surveillance project, managed by the MRU, is nested within a national, laboratory-based surveillance programme (GERMS-SA). The main objective of the project, ongoing since 2005, is to estimate the burden of laboratory-confirmed cryptococcal disease in South Africa. From 1 July 2008, surveillance methodology for the project was changed to reduce the reporting burden on diagnostic laboratories. Only enhanced surveillance sites (25 hospitals in 9 provinces), NHLS laboratories in KwaZulu-Natal, and laboratories in the private, mining, and military sectors were required to directly report case patients to NICD, whereas data from case patients, diagnosed with cryptococcosis at NHLS laboratories in the other 8 provinces, were obtained through an audit of the NHLS Corporate Data Warehouse. In total, 8240 case patients with incident cryptococcosis were detected through the surveillance project in 2008. Cryptococcal isolates (n=1582), obtained from case patients at enhanced surveillance sites, were characterised by phenotypic and genotypic tests at MRU. A detailed report of surveillance findings for 2008 is contained within the GERMS-SA Annual Report 2008. Updated data from the surveillance project (2005 through 2007) were presented at two international conferences and a manuscript, summarising some of these data, was prepared and will be submitted to an international, peer-reviewed journal for publication.

PAEDIATRIC CRYPTOCOCCOSIS

Cases of cryptococcosis in children (<15 years), reported to MRU between 1 January 2005 and 31 December 2007, were compared to adult cases. A large series of paediatric cryptococcal cases was identified and described. During 2008, data from this analysis

were presented at an international conference and a manuscript, summarising these data, was prepared and will be submitted to an international, peer-reviewed journal for publication.

ANTIFUNGAL SUSCEPTIBILITY TESTING OF INCIDENT CRYPTOCOCCAL ISOLATES, 2002-2003 AND 2007-2008

There have been no South African studies examining the prevalence of fluconazole non-susceptibility amongst incident episode isolates of *Cryptococcus* species. Population-based, laboratory-based surveillance for cryptococcosis, initiated in Gauteng in March 2002 and expanded nationally in 2005, provided the opportunity for this issue to be explored further. Clinical strains of *Cryptococcus* species were submitted to the NICD, phenotypically characterised and stored at -70°C to maintain viability. We randomly chose 500 incident episode strains from surveillance case patients, diagnosed with cryptococcosis during 2 time periods (2002-2003 and 2007-2008), for fluconazole minimum inhibitory concentration (MIC) determination by various test methods. Laboratory work for the study will commence in 2009.

MOLECULAR EPIDEMIOLOGY OF ENVIRONMENTAL AND CLINICAL CRYPTOCOCCAL ISOLATES

Isolates obtained from the environment as well as clinical surveillance isolates (obtained from adults and children) were characterised genotypically, in collaboration with investigators at Duke University Medical Center, USA. In 2008, these data were presented at an international conference.

ESTIMATION OF THE CURRENT GLOBAL BURDEN OF CRYPTOCOCCAL MENINGITIS AMONG PERSONS LIVING WITH HIV/AIDS

Cryptococcal meningitis is an important, AIDS-related opportunistic infection, especially in the developing world. In order to assist with development of global strategies and priorities for prevention and treatment, it is important to estimate the burden of disease. In collaboration with investigators at the Centers for Disease Control and Prevention, Atlanta, data from published studies were used to estimate the global burden of cryptococcal meningitis. Data from this study were presented at two international conferences and a manuscript was submitted to an international, peer-reviewed journal for publication.

TRAC-SOUTH AFRICA (TRACKING RESISTANCE TO ANTIFUNGAL DRUGS FOR *CANDIDA* SPECIES IN SOUTH AFRICA): A LABORATORY-BASED SENTINEL SURVEILLANCE PROJECT FOR CANDIDAEMIA AND ANTIFUNGAL DRUG RESISTANCE IN SOUTH AFRICA, 2009-2010

During 2008, a laboratory-based, sentinel surveillance project was designed by MRU, in collaboration with 20 public and private laboratory sites across South Africa, and the Centers for Disease Control and Prevention, Atlanta. The major objective of this project is to describe the species distribution of *Candida* spp. causing bloodstream infection at sentinel sites in South Africa, and to compare the species distribution during 2009-2010, to previous reports and between the public- and private-health sectors. Another major objective is to describe the prevalence of resistance to at least four antifungal drugs (fluconazole, voriconazole, amphotericin B, caspofungin), amongst invasive *Candida* spp. in 2009-2010, and to compare these antifungal drug resistance patterns to previous reports, where possible, and between the public- and private-health sectors. Formal surveillance is anticipated to start on 1 February 2009.

CRYPTOCOCCOSIS AND TUBERCULOSIS (TB) CO-INFECTION AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL, SOUTH AFRICA, JANUARY 2005 TO DECEMBER 2007: A RECORD REVIEW

The main objectives of this cross-sectional, retrospective study were to describe patients at Charlotte Maxeke Johannesburg Academic Hospital, who were treated for both cryptococcosis and TB between 2005 and 2007, in terms of demography, method of diagnosis, treatment and outcome of cryptococcosis, and to define the basis for the TB diagnosis amongst these patients and to categorise according to the strength of TB diagnosis. The findings of this record review were summarised by Lucy Wight in a report submitted in partial fulfilment of the requirements for the degree of MSc in Control of Infectious Diseases at the London School of Hygiene and Tropical Medicine.

MYCOLOGY EXTERNAL QUALITY ASSESSMENT (MEQA) PROGRAMME

In 2008, the MRU coordinated 3 MEQA surveys for 104 laboratories participating in the yeast sub-programme and 49 laboratories participating in the mould sub-programme. Results of laboratory performance are available in summary format in a separate report.

SANAS ACCREDITATION

In 2008, the MRU surveillance laboratory was re-accredited by SANAS in accordance with ISO15189 standards.

COLLABORATIONS

Listing of collaborating institutions/individuals and the appropriate project/programmes.

The GERMS-SA Cryptococcal Surveillance Project

Loekie Badenhorst, MBBCh, FCPATH (SA) Micro, Universitas Hospital/ NHLS

Kosie le Roux, MBBCh, Universitas Hospital/ NHLS

Andrew Rampe, Dip Med Tech, Rustenberg Hospital/ NHLS

Pieter Jooste, FCPaed (SA), Kimberley Hospital

Ken Hamese, FCPaed (SA), Polokwane/ Mankweng Hospital

Jacob Lebudi, Business Manager, Rob Ferreira/ NHLS

Greta Hoyland, Dip Med Tech, Rob Ferreira/ NHLS

Yacoob Coovadia, MBBCh, FCPATH (SA) Micro, Inkosi

Albert Luthuli Hospital/ NHLS

Sindiswe Sithole, MBBCh, Inkosi Albert Luthuli Hospital/ NHLS

Sumayya Haffejee, MBBCh, FCPATH (SA) Micro, Grey's Hospital/ NHLS

Halima Dawood, FCP (SA), Grey's Hospital

Anwar Hoosen, MBBCh, FCPATH (SA) Micro, Steve Biko (Pretoria) Academic Hospital Complex/ NHLS

Kathy Lindeque, Dip Med Tech, Steve Biko (Pretoria) Academic Hospital Complex/ NHLS

Maphoshane Nchabaleng, MBBCh, MMed (Pathology) Microbiology, Dr George Mukhari Hospital/ NHLS

Siseko Martin, MBChB, Tygerberg Academic Hospital/ NHLS & University of Stellenbosch

Elizabeth Wasserman, MBChB, MMed (Path) Microbiology, Tygerberg Academic Hospital/ NHLS & University of Stellenbosch

Olga Perovic, MD, FCPATH (SA) Micro, Charlotte Maxeke (Johannesburg) Academic Hospital/ NHLS

Charles Feldman, MBBCh, FCP (SA), PhD, Charlotte Maxeke (Johannesburg) Academic Hospital/ NHLS

Sandeep Vasaikar, MD, Nelson Mandela Academic Hospital/ NHLS

Vivek Bhatt, MD, Nelson Mandela Academic Hospital/ NHLS

Jeannette Wadula, MBBCh, FCPATH (SA) Micro, Chris Hani Baragwanath Hospital/ NHLS

Alan Karstaedt, MBBCh, FCP (SA), Chris Hani Baragwanath Hospital

Andrew Whitelaw, MBBCh, FCPATH (SA) Micro, Groote Schuur Hospital/ NHLS

Adrian Brink, MBBCh, FCPATH (SA) Micro, Johannesburg, Ampath National Laboratory Services

Maria Botha, MBBCh, FCPATH (SA) Micro, Johannesburg (Metalbox), Ampath National Laboratory Services

Suzy Budavari, MBBCh, FCPATH (SA) Micro, Johannesburg (Sunninghill), Ampath National Laboratory Services

Mark Cruz da Silva, MBBCh, FCPATH (SA) Micro, Johannesburg (Metal Box), Ampath National Laboratory Services

Xoliswa Poswa, MBBCh, FCPATH (SA) Micro, Johannesburg (Pomona), Ampath National Laboratory Services

Inge Zietsman, MBBCh, FCPATH (SA) Micro, Johannesburg, Ampath National Laboratory Services
Juanita Smit, MBBCh, FCPATH (SA), Lancet laboratories

Antifungal Susceptibility Testing of Incident Cryptococcal Isolates, 2002-2003 and 2007-2008

Shawn Lockhart, PhD, Head of Antifungal Drug Testing Unit, Mycotic Diseases Branch, Division of Foodborne, Bacterial and Mycotic Diseases, Centers for Disease Control, Atlanta, USA

Tom Chiller, MD, MPH, Deputy Chief, Mycotic Diseases Branch, Division of Foodborne, Bacterial and Mycotic Diseases, Centers for Disease Control, Atlanta, USA

Molecular Epidemiology of Environmental and Clinical Cryptococcal Isolates

Thomas G. Mitchell, PhD, Associate Professor, Department of Molecular Genetics and Microbiology, Director, Molecular Mycology and Pathogenesis Training Program, Duke University, North Carolina, USA

Anastacia Litvintseva, PhD, Department of Molecular Genetics and Microbiology, Duke University, North Carolina, USA

Kathleen Miglia, PhD, Department of Molecular Genetics and Microbiology, Duke University, North Carolina, USA

Estimation of the Current Global Burden of Cryptococcal Meningitis among Persons Living With HIV/AIDS

Benjamin Park, MD, MPH, Mycotic Diseases Branch, Division of Foodborne, Bacterial and Mycotic Diseases, Centers for Disease Control, Atlanta, USA

Kathleen Wannemuehler, Biostatistics Office, Division of Foodborne, Bacterial and Mycotic Diseases, Centers for Disease Control, Atlanta, USA

Tom Chiller, MD, MPH, Deputy Chief, Mycotic Diseases Branch, Division of Foodborne, Bacterial and Mycotic Diseases, Centers for Disease Control, Atlanta, USA

Barbara Marston, MD, Global AIDS Program, Centers for Disease Control, Atlanta, USA

Peter Pappas, MD, University of Alabama at Birmingham, Birmingham, Alabama, USA

TRAC-South Africa (Tracking Resistance to Antifungal drugs for Candida species in South Africa): A Laboratory-based Sentinel Surveillance Project for Candidaemia and Antifungal Drug Resistance in South Africa, 2009-2010

Inge Zietsman, MBBCh, FCPATH (SA) Micro, Johannesburg, Ampath National Laboratory Services
Loekie Badenhorst, MBBCh, FCPATH (SA) Micro, Universitas Hospital/ NHLS

Yacoob Coovadia, MBBCh, FCPATH (SA) Micro, Inkosi Albert Luthuli Hospital/ NHLS

Adriano Duse, MBBCh, FCPATH (SA) Micro, Johannesburg Hospital/ NHLS

Sumayya Haffjee, MBBCh, FCPATH (SA) Micro, Grey's Hospital/ NHLS

Anwar Hoosen, MBBCh, FCPATH (SA) Micro, Steve

Biko (Pretoria) Academic Hospital Complex/ NHLS
Ranmini Kularatne, MBBCh, FCPATH (SA) Micro, Helen Joseph & Coronation/ NHLS

Maphoshane Nchabaleng, MBBCh, MMed (Pathology) Microbiology, Dr George Mukhari Hospital/ NHLS

Heidi Orth, MBChB, MMed (Path) Microbiology, Tygerberg Academic Hospital/ NHLS & University of Stellenbosch

Olga Perovic, MD, FCPATH (SA) Micro, Charlotte Maxeke (Johannesburg) Academic Hospital/ NHLS

John Simpson, MBBCh, FCPATH (SA) Micro, NHLS Greenpoint laboratory

Sandeep Vasaikar, MD, Nelson Mandela Academic Hospital/ NHLS

Jeannette Wadula, MBBCh, FCPATH (SA) Micro, Chris Hani Baragwanath Hospital/ NHLS

Andrew Whitelaw, MBBCh, FCPATH (SA) Micro, Grootte Schuur Hospital/ NHLS

Adrian Brink, MBBCh, FCPATH (SA) Micro, Johannesburg, Ampath National Laboratory Services

Maria Botha, MBBCh, FCPATH (SA) Micro, Johannesburg (Metalbox), Ampath National Laboratory Services

Suzy Budavari, MBBCh, FCPATH (SA) Micro, Johannesburg (Sunninghill), Ampath National Laboratory Services

Mark Cruz da Silva, MBBCh, FCPATH (SA) Micro, Johannesburg (Metal Box), Ampath National Laboratory Services

Chris Jansen van Rensburg, BSc (Hons), MBBCh, MMed (Path) Microbiology, Bloemfontein, Van Rensburg Pathologists

Nolan Jansen van Rensburg, MBBCh, F. C. Path (SA) Micro, Bloemfontein, Ampath National Laboratory Services

Norman Miller, MBBCh, FCPATH (SA) Micro, Durban, Ampath National Laboratory Services

Johan Moolman MBBCh, FCPATH (SA) Micro, Lancet Laboratories

Xoliswa Poswa, MBBCh, FCPATH (SA) Micro, Johannesburg (Pomona), Ampath National Laboratory Services

Ben Prinsloo, MBChB, MMed (Path) Microbiology, Vermaak and Partners

Marthinus Senekal, MBBCh, FCPATH (SA) Micro, Cape Town, Pathcare Laboratories

Peter Smith, MBChB, MMed (Path) (Microbiology), Bloemfontein/ Kroonstad/ Welkom/ East London, Ampath National Laboratory Services

Johan van Greune, MBBCh, FCPATH (SA) Micro, Cape Town, Ampath National Laboratory Services

Gerhard Weldhagen, MBChB, MMed (Path) (Microbiology), PhD, MASM, Pretoria, Ampath National Laboratory Services

Tom Chiller, MD, MPH, Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, USA

Shawn Lockhart, PhD, Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, USA

Guy Richards, MBBCh, FCP (SA), Charlotte Maxeke (Johannesburg) Academic Hospital

Mervyn Mer, MBBCh, FCP (SA), Charlotte Maxeke (Johannesburg) Academic Hospital

Cryptococcosis and tuberculosis co-infection at Charlotte Maxeke Johannesburg Academic Hospital, South Africa, January 2005 to December 2007: a record review

Lucy Wight, London School of Hygiene and Tropical Medicine, United Kingdom

Kerrigan McCarthy, MBBCh, FCPATH (SA), Reproductive Health and HIV Research Unit, South Africa

Francois Venter, MBBCh, FCP (SA), Reproductive Health and HIV Research Unit, South Africa

Olga Perovic, MD, FCPATH (SA) Micro, Charlotte Maxeke (Johannesburg) Academic Hospital/ NHLS

Charles Feldman, MBBCh, FCP (SA), PhD, Charlotte Maxeke (Johannesburg) Academic Hospital/ NHLS

Alison Grant, MBBS, London School of Hygiene and Tropical Medicine, United Kingdom

CAPACITY BUILDING

Xoliswa Poswa, MSc Epidemiology, School of Public Health, University of the Witwatersrand, Johannesburg. Dissertation Title: In-hospital mortality of HIV-associated cryptococcal disease in patients treated with amphotericin B versus fluconazole
Supervisors: Nelesh Govender & Cheryl Cohen

PATHOLOGY REGISTRAR TRAINING

The MRU participated in the NICD training programme for pathology registrars. In 2008, 12 clinical pathology and mono-speciality registrars were trained for a day (8 July) as part of the short training programme, and 5 mono-speciality registrars were trained for 1 week (1-5 April and 11-15 August) as part of the long programme. Training included practical identification of clinically important yeasts and moulds, a review of antifungal susceptibility test methods, an introduction to molecular epidemiology and molecular diagnostic techniques as well as an overview of relevant clinical infectious disease issues.

ADVANCED MYCOLOGY WORKSHOP, 24-28 NOVEMBER 2008

The week-long workshop aimed to establish expertise in mycology laboratory techniques in referral diagnostic laboratories in South Africa, and was primarily intended to provide laboratory workers with the skills to identify clinically important fungi and to understand the major concepts required for performance, quality control and interpretation of antifungal drug susceptibility testing. During 24-28 November 2008, 4 laboratory workers attended the course: 2 (NHLS Groote Schuur Hospital), 1 (NHLS Charlotte Maxeke Johannesburg Academic Hospital) and 1 (Ethiopia).



Figure 1: Participants in the Advanced Mycology Workshop, Mycology Reference Unit, 24-28 November 2008