

University of the Free State



Department of Anatomical Pathology

Head: **Prof Bruce Middlecote**

Diagnostic services

The department provides a diagnostic surgical pathology service to all the provincial hospitals in the Free State, and from May 2008 onwards, to some of the provincial hospitals in the North West Province. From time to time, work was also sent from the Northern Cape. A cytopathology service was provided to the Free State and Northern Cape. During the year, 21,685 surgical pathology cases and 51,400 cytopathology cases were seen.

Research projects

A profile of neurofibromatosis type I in the Free State

Researchers: Prof CA Beukes, Dr BD Henderson, Dr J Goedhals, Dr PJ Swart

This is a multidisciplinary study to establish the incidence of neurofibromatosis in the Free State, as well as to define the local disease profile.

The association between penile carcinoma and HIV

Researchers: Dr J Goedhals, Dr J Thiart, Prof CA Beukes

Penile carcinoma appears to have become more common during the last decade. This study aims to establish the importance of HIV as an aetiological agent or risk factor.

The quality of specimens obtained by fine needle aspiration: does training make a difference?

Investigators: Dr J Goedhals, Prof CA Beukes, Prof G Joubert, Prof CA Wright

The importance of sample qualities and smear preparation is not well recognised. No formal training in fine needle aspiration technique is given to medical students at the University of the Free State. The aim of this study is to determine if training in fine needle aspiration technique will improve the adequacy of aspirates performed by clinicians.

Teaching and training

Undergraduate

The department presents a module on general pathology to the second year medical students. Sessions on systematic pathology, which are integrated into system modules, are conducted with both second and third year students. The total contact time is approximately 140 hours per year.

Postgraduate

Daily departmental and interdepartmental meetings are held. Registrars from Forensic Pathology rotate through the department for two years. Registrars from Oncotherapy each spend four months in the department.

Honours

At the autumn graduation ceremony of the University of the Free State, Dr VA Yazbek received the following awards: The Dean's medal for best postgraduate student in the Faculty of Health Sciences in 2007, and the Senate medal for best masters student at the University of the Free State in 2007.

Research output

Published publications: 1
Conference presentations:
International: 1
National: 3

Professional development

Number of registrars in department: 6
Number of registrars successfully completing studies: 1

Department of Chemical Pathology

Acting head: **Prof Johannes Kuyl**

Consultants and registrars have moved into the renovated office wing of the department, which includes a research and training laboratory. The renovated seminar room has been fitted with computer-projector combination linked to the medical school internal network.

Diagnostic services

The routine laboratory processed approximately 200,000 specimens, doing about 700,000 tests, during the year. Specimens were mostly from Universitas Hospital, National Hospital and 3 Military Hospital. Specimens are also referred from Pelonomi and Kimberley laboratories. Consultants and registrars attend the endocrine, lipid and diabetic clinics on a regular basis. A consultant or registrar visited Kimberley laboratory once a month during the year. The laboratory is preparing for SANAS accreditation in 2009.

Research projects

- Biochemical, nutritional and medical profile of the rural population of the Free State
Researchers: Dr H van Wyk, Dr A Groenewald and the Department of Human Nutrition
- Biochemical changes in males undergoing prostatectomy and orchidectomy
Researchers: Dr H van Wyk, Dr A Groenewald and the Department of Urology
- Cross-reactivity of the insulin immunoassay with the various commercial recombinant human insulins
Researcher: Dr D Schulenburg

Teaching and training

The department is involved in undergraduate and postgraduate training. Lectures are given to a broad spectrum of students ranging from technologists, medical undergraduates to registrars in surgery, internal medicine and anaesthesiology. Part of postgraduate training is the weekly seminars and a journal club to which registrars and consultants from the clinical departments are also invited.

Research output

Published publications: 1
National conference presentations: 3

Professional development

Postgraduate candidates graduated: 1 (MMed (Chem Path))
Postgraduate candidates enrolled: 3 (MMed (Chem Path))

Department of Haematology and Cell Biology

Head: **Prof Phillip Badenhorst**

The Department of Haematology and Cell Biology comprises the divisions of haematology, immunology and molecular biology. The latter includes a genetically modified organisms (GMO) testing facility.

Diagnostic services

The department renders diagnostic services to Universitas Hospital and its satellite laboratories situated on the premises of National and 3 Military hospitals. The laboratory also serves as a reference laboratory for the Free State and Northern Cape provinces and reports bone marrow aspirations and trephine biopsies for the outlying laboratories in the region. A total of 109,140 specimen analyses were performed during the year.

Apart from diagnostic services, consultants and registrars also render clinical services in the form of a haematology clinic, a thrombophilia clinic, a haemophilia clinic, an oral anticoagulation clinic, as well as outreach clinics at Bethlehem, Welkom and Kimberley hospitals. The various clinics involved 12,440 patient visits for the year.

One of the registrars visits the laboratory at Pelonomi Hospital on a daily basis, including Saturdays and Sundays to review blood smears, perform bone marrow aspirations, do telephonic and ward consultations, and render advice to and write out prescriptions for the oral anticoagulation clinic.

The GMO testing facility is the only laboratory in Africa where DNA-based GMO testing is done using real-time polymerase chain reaction technology. During the year, 686 specimens were tested. This facility also makes an important contribution to research regarding GMO detection in food and its safety.

Research

Sources of research funding

Research is funded by the NHLS Research Trust, the University of the Free State, the South African Medical Research Council, the National Research Foundation, research contracts with private companies and international collaboration agreements. The latter include the Hungarian-South African Collaboration Agreement, the Flemish-South African Collaboration Agreement, and the ABLYNX, Thromb X and Glenmark contract research agreements.

Research projects

New projects initiated this year are:

ADAMTS13 levels in HIV-infected patients with and without TTP

Researchers: Prof M Meiring, Prof PN Badenhorst, Prof H Deckmyn

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening disease characterised by microvascular platelet deposition and thrombus formation in selected organs with resulting microangiopathic haemolytic anaemia, thrombocytopenia, neurological symptoms, and renal failure. Typically a very rare disorder, TTP is being seen with increased frequency in patients infected with HIV. Deficiency of the von Willebrand factor cleavage protease, also known as ADAMTS13, has been implicated as a major aetiological factor in TTP. However, before studying the role of ADAMTS13 in HIV-related TTP, it is necessary to know the normal values of ADAMTS13 levels in the population group in question because lower ADAMTS13 levels had been reported in other populations such as the Chinese. It is also necessary to know whether HIV infection in the absence of TTP has any effect on ADAMTS13 levels. The aim of the study is three-fold: a) to compare the ADAMTS13 levels in the local Caucasian and African populations; b) to study the effect of HIV infection on ADAMTS13 levels by correlating CD4 counts and viral loads with ADAMTS13 levels in HIV-positive patients without TTP; and c) to measure ADAMTS13 levels in HIV-infected patients with TTP.

Von Willebrand factor clearance in type 1 von Willebrand disease

Researchers: Prof M Meiring, Ms P Setlaba

The aim of this study is to develop a cost-effective ELISA to determine the von Willebrand factor (VWF) propeptide levels in the stored plasmas of type 1 von Willebrand disease patients and to calculate the half-life of VWF in these patients. A further aim is to develop a method in order to search for known mutations that cause decreased survival of VWF in patients with an increased VWF propeptide/VWF antigen ratio.

Development of cost-effective von Willebrand factor and ADAMTS13 level and -activity assays

Researchers: Prof M Meiring, Mr TC Motsoeneng, Ms Ngidi

The aim is to select ADAMTS13 binding antibodies by using phage display technology in order to develop a cost-effective laboratory test for the determination of ADAMTS13 levels in plasma. The second aim is to set up an assay to study the activity of ADAMTS13. The current collagen binding assay will be modified to be used to measure ADAMTS13 activity. The third aim is to introduce a more sensitive and cost-effective ristocetin cofactor assay in von Willebrand disease diagnostic workup using flow cytometry. A further aim is to adjust the current assays for von Willebrand factor (VWF) levels and collagen-binding activity in order to measure extremely high VWF levels and activity.

Relationship between inflammation, coagulation, von Willebrand factor and ADAMTS13

Researchers: Prof M Meiring, Ms E le Roux, Mr W Allers

The aim of the study is to determine the ultra large von Willebrand factor (VWF) levels and activity, VWF propeptide levels, ADAMTS13 levels and activity and ADAMTS13 mRNA expression in cultured human aortic endothelial cells upon stimulation with inflammatory cytokines such as interleukin-6 (IL-6), IL-8, interferon- γ , tumour necrosis factor- α and tissue factor (TF) or thrombin. The second aim of this study is to determine the levels and activities of TF, VWF and ADAMTS13, VWF propeptide levels as well as mRNA levels of ADAMTS13 within microparticles derived from the cultured endothelial cells stimulated with inflammatory cytokines.

JAK2 and exon 12 mutations and its significance in myeloproliferative disorders

Researchers: Mr QC Goodyear, Dr A de Kock

Myeloproliferative neoplasms are haematological disorders in which there is an increase in proliferation of cells in the myeloid lineage. JAK2 mutations in exon 14 and 12 have been identified in several of these disorders such as polycythaemia vera, essential thrombocytosis and myelofibrosis. In the study, 53 patients with various myeloproliferative neoplasms were screened by sequencing for exon 12 mutations and a control group of nine individuals was added. No mutations in exon 12 were found; however, a deletion was found in intron 13 in a large percentage of the patients.

JAK2 V617F mutation in myeloproliferative neoplasms

Researchers: Mr M Madzime, Dr A de Kock

Myeloproliferative neoplasms (MPNs) are characterised by over-proliferation of myeloid lineages and include polycythaemia vera, essential thrombocythaemia, idiopathic myelofibrosis, chronic myeloid leukaemia (CML) as well as minor forms. All but typical CML are associated with the JAK2V617F mutation. This mutation has become an important diagnostic biomarker; however, it is absent in other MPNs. This study, therefore, screened exon 14 of the JAK 2 gene for non-JAK2V617F mutations which might also be involved in MPNs. The study used blood fixed on FTA cards to obtain genomic DNA following which PCR was used to amplify exon 14 and portions of introns 14 and 15. The PCR products were electrophoresed and the gel viewed under ultra violet light. 364bp fragments were stabbed out and submerged in 100 μ l of ultra pure water then incubated at 4°C overnight. The purified PCR products were sequenced and three non-JAK2V617F mutations were found, one of which might be important in MPN pathogenesis.

MicroRNA expression profiling analysis in myeloproliferative neoplasms

Researchers: Ms CB Winson, Dr A de Kock

MicroRNAs (miRNAs) are non-coding, single RNA strands that are 18-23 nucleotides in length. These small RNAs are able to regulate processes like developmental timing, haematopoietic differentiation, apoptosis, cell proliferation and organ development, through the regulation of the expression of genes at the post-transcriptional level. MiRNA profiling through techniques like microarrays and quantitative reverse transcription PCR, has revealed unique miRNA signatures in the haematopoietic malignant disorders called the myeloproliferative neoplasms (MPNs). Polycythaemia vera (PV) is one of these MPNs and is a clonal stem cell disorder, characterised by the overproduction and proliferation of erythrocytes. The miRNA profiles found in PV and the MPNs represent the upregulation or downregulation of specific miRNAs compared to normal tissue miRNA profiles. The contribution of the differentially expressed miRNAs to the myeloproliferation in the MPNs can be explained through the role of miRNAs as tumour suppressors that may be down-regulated or as oncogenes that can be up-regulated. In this project the aim is to profile patients diagnosed with PV through quantitative real time PCR, so that possible miRNA patterns in these patients can be established. Further investigation into these patterns will increase the understanding of the pathogenesis behind PV and will possibly provide a new diagnostic tool for the identification of PV in the future and might also serve as a therapeutic tool to help those suffering from PV.

Teaching and training

The department is involved in undergraduate teaching and training of medical students and scientists and is either responsible for or contributes to various modules in the different phases of the new curriculum. Apart from training registrars in haematology and clinical pathology, the department also supervises honours, masters and doctorate candidates. The department also trains medical technologists.

Honours

Prof M Meiring won the Muller Potgieter Medal for the best publication in laboratory research for the publication 'Performance and utility of a cost-effective collagen-binding assay for the laboratory diagnosis of von Willebrand disease'.

Prof C Viljoen was runner-up for the best paper in laboratory research (senior category) at the Faculty Forum, Faculty of Health Sciences, for his paper entitled 'Improving copy number detection during real-time PCR quantification with dual gene specific cDNA synthesis'.

Mr JJ van Deventer won the prize for the best paper in laboratory research (junior category) at the Faculty Forum, Faculty of Health Sciences, for his paper entitled 'The application of real-time quantitative PCR in CML diagnostics'.

Ms S Screenivasan was runner-up for the best paper in laboratory research (junior category) at the Faculty Forum, Faculty of Health Sciences, for her paper entitled 'The detection of point mutations conferring resistance to imatinib in patients with chronic myeloid leukaemia'.

Dr W Chen was runner-up for the best poster in laboratory research (senior category) at the Faculty Forum, Faculty of Health Sciences for his poster entitled 'The effect of curcumin on the cytotoxicity of leukaemia cells and normal peripheral blood mononuclear cells'.

Ms M Kelderman was runner-up for the best poster in laboratory research (junior category) at the Faculty Forum, Faculty of Health Sciences for her poster entitled 'The Von Willebrand disease testing facility in Bloemfontein'.

Research output

Publications published: 7
Conference presentations:
International: 6
National: 14
Local: 15

Professional development

There are five registrars specialising in haematology of whom three passed the primary examination for the MMed degree (one with distinction). Three scientists have been appointed to intern posts. Eleven students have enrolled for the BMedSc honours programme (five in haematology and six in molecular biology). There are six MMedSc and two PhD students.

Division of Human Genetics

Head: **Prof Magda Theron**

Diagnostic services

The division provides almost all human genetics services to the Northern Cape and most parts of the Free State. The laboratories primarily render a comprehensive diagnostic service to the Universitas Hospital, 3 Military Hospital, Pelonomi Hospital, Kimberley Hospital, Upington Hospital, surrounding clinics and various private pathology firms. Comprehensive medical genetics encompass four sub-disciplines: molecular genetics, molecular cytogenetics (or fluorescent *in situ* hybridisation (FISH)), cytogenetics and clinical genetics.

Mutation screening in the molecular genetic laboratory is mostly polymerase chain reaction (PCR)-based and population-directed. The division provides an extensive routine diagnostic screening for inherited breast cancer and referrals throughout South Africa are diagnosed. The FISH laboratory renders a pre- and postnatal screening programme based on microdeletions and common chromosomal aneuploidies. The cytogenetics laboratory provides a pre- and postnatal laboratory service for congenital and acquired chromosomal abnormalities. Cytogenetic analysis plays a major role in the diagnosis, prognosis and treatment of acquired genetic aberrations associated with haematological malignancies. Traditional cytogenetic analysis is performed on peripheral blood, bone marrow, amniotic fluid, products of conception and skin fibroblasts.

The department is SANAS-accredited and a HPCSA-accredited intern medical scientists training facility.

Research

Research interest in 2008 mainly revolved around the evaluation of modifiable genetic risk factors which may be of considerable importance in the management of inherited breast cancer patients. The identification of modifier genes that may influence the clinical expression of common single gene disorders is of fundamental importance for genetic counseling, prognostic value and treatment strategies. Failure to demonstrate significant differences in allelic distribution between mutation carriers with and without disease reflect the difficulty in defining minor gene effects in the presence of a major gene defect.

Research project

Search for genetic modifiers of cancer risk and penetrance conferred by BRCA2: targeting DNA repair polymorphisms

Researchers: Dr NC van der Merwe, Prof M Theron, Mr B Delport

Funding: NHLS Research Trust

Carriers of the mutated BRCA2 gene (c.8162delG) are at an increased risk for developing breast and/or ovarian

cancer; however, penetrance estimates differ. Modification of the risk by other genes clustering in families could explain most of this difference. Genes involved in DNA repair which interact and co-localises with the BRCA1 and 2 proteins (RAD51 and BARD1) are of particular interest since together they participate in DNA double-strand break repair through homologous recombination. Polymorphisms in these genes may modify breast cancer risk in germline BRCA mutation carriers. The aim of this study was to determine whether these ancient variants could elucidate the residual risk associated with the founder BRCA 2 mutation in the Afrikaner. The SNP in exon 7 of BARD1 was uncommon (6/120) within in the Afrikaner population, while the RAD UTR 135G>C variant was present in the majority of participants (70/120). These variants may explain the residual risk observed for germline BRCA2 mutation carriers in the Afrikaner.

Teaching and training

Medical technologists

Two qualified medical technologists met the entrance requirements of the HPCSA (Board of Medical Technologists) and were registered in the discipline of cytogenetics. The national shortage of qualified technologists posed a challenge to maintain a high quality and acceptable turnaround time diagnostic service in this discipline. In an attempt to counteract and to provide fully qualified professionals in the discipline, all available student medical technologist positions were temporarily converted into intern medical scientist positions.

Intern medical scientists

The division is a HPCSA-accredited training facility for intern medical scientists and the first student completed this newly implemented internship in 2008. Three intern medical scientists are currently enrolled in the internship programme. The vision of the division is the simultaneous incorporation of all intern medical scientists in a full-time Master's or Doctorate programme.

Postgraduate

One MMedSc student has been supervised and qualified.

Outreach programme

The NHLS laboratories in Kimberley and Upington were visited with the primary focus of setting up a referral system and the introduction of the various routine diagnostic services provided by the department.

Honours

The division was awarded with the trophy for the most entries to the Faculty Forum, Faculty of Health Sciences.

Research output

National conference presentations: 10

Department of Medical Microbiology and Virology

Acting head: **Dr Louis Badenhorst**

Diagnostic services

The department provides a 24-hour microbiology and virology consultation service to Universitas, National and Pelonomi hospitals as well as to the rest of the Free State. It also provides information on request to medical practitioners and healthcare workers. Hospital patients are visited and examined on a consultation basis.

A consultant and/or registrar from Universitas visit the Pelonomi laboratory on a daily basis to verify results, and also pay visits to the Kimberley Hospital on a monthly basis. The virology section of the department has seen an enormous growth in the number of HIV viral loads and PCR tests to such an extent that the employment of two extra technologists was necessary.

Research fields and projects

Conventional and molecular techniques are used to investigate the resistance, resistance determinants and molecular epidemiology of organisms with the potential to cause outbreak and epidemics in the community. This group, under Ms A van der Spoel van Dijk, works closely with the Free State Department of Health, serving on provincial and national committees involved in surveillance (sexually transmitted infections) and health programmes (tuberculosis caused by *Mycobacterium tuberculosis*) to assist in fast and effective recognition of developing resistance and outbreaks to ensure timely intervention. Current research projects include:

- Molecular characterisation of *Klebsiella pneumoniae* strains

- Microbiological surveillance of sexually transmitted infections in the Free State
Collaborator: Dr D Lewis (Sexually Transmitted Infections Reference Centre, NICD)
- Investigation of IS6110-RFLP fingerprinted *Mycobacterium tuberculosis* strains from three areas in the Free State to decipher the historic origin of the strains
 - Origin and diversity of *Mycobacterium tuberculosis* strains in the Free State
Project leader: Mr PM Makhoahle
Collaborator: Dr L Rigouts (Prince Leopold Institute of Tropical Medicine, Antwerpen, Belgium)
- Monitoring of drug resistance, drug resistance determinants and molecular epidemiology of *Mycobacterium tuberculosis* isolates in the Free State
 - *Mycobacterium tuberculosis* isolates in the Free State: prevalence of rifampicin (RIF) resistance and characterisation of RIF-resistant strains
 - *Mycobacterium tuberculosis* multidrug-resistant outbreak in the Zastron area, Free State
Collaborators: Prof T Victor (Faculty of Health Sciences, University of Stellenbosch); Dr L Rigouts (Prince Leopold Institute of Tropical Medicine, Antwerpen, Belgium); Free State Department of Health

Research under Prof FJ Burt focuses on characterising humoral and cellular immune responses in patients with Crimean-Congo haemorrhagic fever (CCHF) virus; epitope discovery for vaccine development; development of molecular and serological assays for detection of arboviruses and other neglected diseases; and evaluation of vaccines against CCHF and Rift Valley fever viruses. Current topics include:

- Identification of tick-borne pathogens in humans in southern Africa
- Emerging zoonotic viruses in southern Africa
- Immune responses in Crimean-Congo haemorrhagic fever patients
Collaborators: Prof R Swanepoel, Prof J Paweska (Special Pathogens Unit, NICD)
- Protein microarrays for serological diagnosis of viral infections and other neglected diseases
- Vaccines for Rift Valley fever and CCHF
Collaborators: Prof J Paweska, Prof R Swanepoel (Special Pathogens Unit, NICD); Prof M Heise (Carolina Vaccine Institute, North Carolina, USA); Prof T Ross (University of Pittsburgh, Center for Vaccine Research, Pittsburgh, USA)

Other projects:

- In collaboration with the Department of Otorhinolaryngology, a project is undertaken to identify the subtypes of human papillomavirus associated with recurrent laryngeal papillomas in a cohort of patients from the Free State and to determine if there is an association between subtype and disease aggressiveness.
Collaborators: Dr D Goedhals; Dr I Rossouw, Dr R Seedat and Prof L Louw (Otorhinolaryngology Department).
- A phase II study of gemcitabine and cisplatin in HIV-positive patients with cervical cancer
Investigators: Prof L Goedhals (Department of Oncotherapy); Dr D Goedhals; Dr MJ Strydom (Department of Oncotherapy)
- Drug resistance surveillance and treatment monitoring network for the public sector HIV antiretroviral treatment programme in the Free State
Collaborators: Dr D Goedhals; Dr C Seebregts (Medical Research Council); Dr D Steyn, Dr C van Vuuren (Department of Internal Medicine,); Prof S Cassol (University of Pretoria); Dr T de Oliveira (University of the Western Cape); Dr D Katzenstein (University of Stanford, USA)
- Investigation into T-cell function and viral adaptation in AIDS
Investigators: Dr D Steyn, Dr C van Vuuren (Department of Internal Medicine); Dr D Goedhals; Prof R Phillips, Dr J Frater (University of Oxford, UK)
- The prevalence of corridor disease in the Eastern Cape Province
Principal investigator: Prof A-M. Pretorius
Co-investigator: Dr DM Parker (Wildlife & Reserve Management Research Group, Department of Zoology & Entomology, Rhodes University, Grahamstown)
In this project the hypothesis that *Theileria parva parva* is not present in the Eastern Cape is tested by sampling ticks and mammalian vectors to test for the appropriate antigen.
- Co-infection between bartonella and haemoplasma in HIV-positive patients from South Africa
Principal investigator: Prof A-M Pretorius
Co-investigator: Prof R Birtles (Department of Veterinary Pathology, University of Liverpool, UK) HIV-positive mothers and babies are investigated for co-infection of *Bartonella* and haemoplasmas.
- Rapid, cost-effective diagnosis of tuberculosis
Investigators: Prof H Viljoen, Prof O Chacon, Prof R Barletta (University of Nebraska-Lincoln, Nebraska, USA); Prof A Freifeld, Prof C Gebhart (University of Nebraska Medical Center, USA); Dr J Termaat, Philisa, Inc, USA); Prof A-M Pretorius
The possibility of a rapid, accurate diagnostic tool for the diagnosis of tuberculosis is investigated.
- Determination of dust mite allergens in Bloemfontein areas using the Multiplex ARay for Indoor Allergens MARIA™
Investigators: Prof W Sinclair (Department of Dermatology, University of the Free State); Prof A-M. Pretorius; Ms L Coetzee (National Museum, Bloemfontein)

The array simultaneously measures the mite allergens Der p 1, Der f 1 and mite group 2, animal allergens of cat (Fel d 1), dog (Can f 1), rat (Rat n 1) and mouse (Mus n 1) as well as cockroach (Bla g 2). MARIA™ provides improved assay performance (increased sensitivity, accuracy and precision) in a high throughput system with substantial time and cost savings.

- Epidemiological investigation of tick-borne diseases in ticks from birds from the Free State

Investigators: Prof A-M Pretorius, D de Swardt (National Museum, Bloemfontein)

The role of birds as reservoirs of *Anaplasma phagocytophilum*, *Babesia* spp and *Borrelia burgdorferi* sensu lato is investigated, by using different molecular typing detection methods.

Teaching and training

The department is involved in teaching of undergraduate students, i.e. medical students in the second and third years, optometry first and third years, BSc (Medical Microbiology) third year, as well as postgraduate students, i.e. MMed, Hons and MSc. An introductory medical microbiology course is also presented to physiotherapy and occupational therapy students. All undergraduate lectures are presented in English and Afrikaans. Three MMed registrars are working in Medical Microbiology and one in Virology.

Research output

Publications published: 7

Conference presentations:

International: 4

National: 4

Professional development

Postgraduate candidates enrolled: 5 (3 PhD, 2 MMedSc)