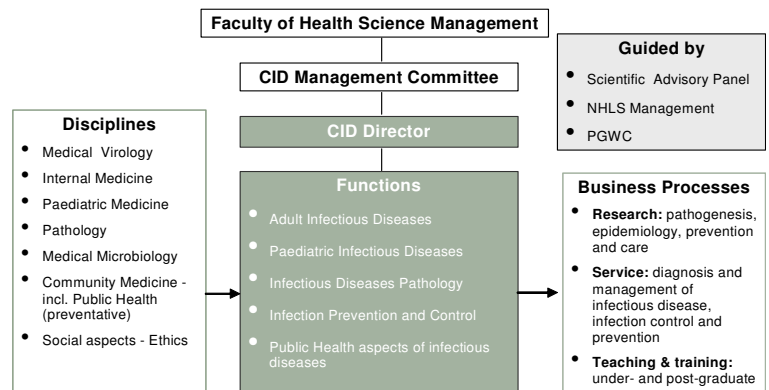


Center for Infectious Diseases
Infeksiesiekte Sentrum
www.sun.ac.za/cid
 CID, Faculty of Health Sciences, Tygerberg, Stellenbosch University

In 2005 academic leaders at the Faculty of Health Sciences (FHS) of Stellenbosch University (SU) representing disciplines focussed on infectious diseases identified the need to formalise their existing synergies into an organizational structure of the Centre for Infectious Diseases (CID). The senate of the University approved the constitution of CID at the end of 2006. The newly established centre is a multidisciplinary academic entity with focus on research, service, teaching and training in infectious diseases.

**Special Interest:**

- Cervical Cancer in HIV+ Women
- Application of Cu²⁺ in IPC

Highlights on page 2:

- ARV drug resistance
- Hypervirulent TB

Cervical Cancer in HIV-positive women: the Next Epidemic?

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Cervical Cancer (CC) is the leading cancer in SA Females. The lifetime risk of CC in South Africa has been reported as 1 in 26. Overseas, HIV positive women have been found to have higher incidence of HPV infection, cervical dysplasia of recurrence thereof. A recommendation that HIV-positive women have yearly PAP smear screening is not widely implemented. With the advent of ARVs becoming more available, it is expected that the life-expectancy will increase 2-3 fold, leaving an emergence opportunity for high-grade dysplasia lesions (HSIL). To investigate the situation at Tygerberg Hospital, we have analyzed the PAP smear -records of 648 HIV-positive females on the ARV program at the clinic. 295 (45.6%) were found to have cytology or pathology results on record at the hospital. Cytological follow-up time was 2,1 year per patient, with 64.4% patients (follow-up) FU time 1 year or less. 80 evaluated patients (27.1%) were found to have LSIL lesions (ASCUS or CIN I), 87 (29.5%) HSIL lesions and 9 (3.1%) had carcinomas. These figures are compared to antenatal statistics from 1997 (100% patients FU time 1 year or less), with LSIL lesions in 2.66% and HSIL lesions in 0.84% of patients. Infections were observed in 116 (39.3%) of evaluated patients, which included 55 (18.6%) Candida, 6 (2.0%) Herpes, 45 (15.3%) Trichomonas and 44 (14.9%) Gardnerella. The lower incidence of infections seen may be ascribed to higher condom use in HIV-infected patients. Although not a prevalence study of abnormal cytological screening in an HIV population, this evaluation describes the necessity for more aggressive screening and FU of HIV-infected patients.

Application of copper and its alloys in Infection Prevention and Control

Prof Shaheen Mehtar, Dr Ian Wiid, Dr. Svetoslav Todorov

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The Unit for IPC in collaboration with Dept of Microbiology, and Dept of Molecular Biology and Human Genetics undertook an in-vitro study examining copper and its alloys against clinical isolates of nosocomial pathogens. Methicillin resistant *Staphylococcus aureus* (MRSA), *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Candida albicans* and *Mycobacterium tuberculosis* were tested against copper and its alloys. Stainless steel and PVC were included as controls. The aim of the study was to determine the amount of copper required to inhibit most nosocomial isolates at room temperature (RT) and at 4°C. At RT, the inhibitory activity of copper (Cu), DZR and Brass 70/30 against *C. albicans* and *K. pneumoniae* was noted at 60 min and with nickel silver (NiAg) against *C. albicans* at 60 min and *K. pneumoniae* at 270 mins. Brass 70/30 and NiAg inhibited *P. aeruginosa* at 180 min and at 270 mins with Cu and DZR. Copper and DZR inhibited *A. baumannii* at 180 min while the other alloys were effective at 360 min. Stainless steel and PVC showed little or no inhibitory activity. At 4°C, the inhibitory activity of copper and its alloys was much reduced. Two strains of *M. tuberculosis*, one isoniazid resistant (R267) and the other multiply drug resistant (R432) showed Growth Inhibition (GI) with Cu of 98% and 88% respectively compared with PVC; the other alloys had an average inhibition of 75% and 30% respectively. Time to Positivity (TTP) for R267 was greater than 15d with Cu and 11d for the other alloys; with R432 it was 5d. Effective inhibition of nosocomial pathogens and MTB by Cu and alloys containing >55% of copper supports its use in reducing environmental bioburden. The study has been extended to its application in a primary healthcare clinic in Grabouw where a controlled study on the impact of environmental bioburden is currently underway. The activity of copper against MTB is being investigated in the cough room of the Infectious Diseases Clinic. It is envisaged that these results will advise the International Copper Association on the levels of copper suitable for surfaces in health care environment. However, a major drawback is the tarnishing property of copper which leaves surfaces looking unsightly. Non tarnishing surfaces incorporating copper are being investigated and will be tested in the future.

HIV antiretroviral drug resistance – an emerging problem for South Africa?

Gert van Zyl, Susan Engelbrecht, Wolfgang Preiser

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Background

An estimated 6 million South Africans live with HIV/AIDS. So far, only about 300,000 receive antiretroviral therapy (ART), with another 500,000 urgently needing treatment. Nevertheless, the national ART roll-out programme which started in 2004 is gathering pace, and will result in unprecedented numbers of patients on ART. Patients who start ART receive a first-line triple drug regimen which is low-cost and usually fairly well tolerated. However, it requires a very high level of adherence in order to prevent the emergence of antiretroviral resistance. Personal, sociological and economic factors can affect drug adherence. There are also medical causes, such as diarrhoea or concurrent use of antituberculosis drugs, that can lead to insufficient plasma levels of antiretroviral drugs. Inadequate drug levels are the primary cause for the development of resistance in patients on therapy. Due to the high error rate and lack of proofreading ability of the viral reverse transcriptase, virus variants with mutations conferring drug resistance arise on an ongoing basis within infected individuals. When ART does not fully suppress viral replication, such resistant virus variants that arise by chance gain a selective advantage. The use of single-dose nevirapine (NVP) for the prevention of mother-to-child transmission (PMTCT) is associated with a high risk of NVP resistance in mothers. One must distinguish between transmitted resistance (when a resistant HIV strain is transmitted, as in 10 – 20% of new infections in some European studies) and acquired resistance (induced by suboptimal drug treatment of infected patients).

Resistance-related research at Medical Virology Tygerberg

1. Development of an affordable *in house* resistance test. Antiretroviral resistance testing, usually done by genotypic analysis, is a valuable diagnostic tool. It can provide information that enables appropriate selection of therapy regimens in naïve patients initiating ART, drug-experienced patients failing on ART and also to determine the prevalence of transmitted resistance in a population. However the widespread use of resistance testing is precluded by the high price of commercial assays and their high demands on staff expertise and equipment. We recently adapted, optimised and evaluated an *in house* resistance test for use in our setting. Being based on PCR and sequencing, it is very similar to commercial assays and still highly demanding. However, it allows resistance testing at a much more affordable price than before. New alternatives will in future be investigated to further reduce costs, e.g. by obviating the need for sequencing.

2. Resistance arising in the Western Cape PMTCT programme. The Western Cape Province is the only South African province where a drug combination is used for PMTCT. HIV-infected mothers receive zidovudine (AZT) from 34 weeks gestational age and single-dose NVP during labour; their babies receive a single dose of NVP and 7 days of AZT. We collected maternal blood samples at baseline and at the closest visit to six weeks after birth in women attending antenatal clinics at Tygerberg Hospital and Delft Community Health Care. Of 76 women tested, 13 (17.1%) acquired NVP resistance after this intervention. This is lower than resistance after NVP alone which varies between 25% and 69% in different studies.

3. Resistance evolution in patients on therapy. In a newly commenced study funded by the South African National Department of Health, we will monitor the development of resistance in the Tygerberg HIV Family Clinic. Various patient factors will be correlated with the development of resistance. Due to the limited availability of antiretroviral drugs, conservative criteria for regimen switch and the presence of clinical benefit of therapy even in patients showing virological failure (as measured by viral load) on ART, patients are often retained on failing antiretroviral regimens for prolonged periods. We will investigate the evolution of resistance in patients on ART in an attempt to determine the impact of the current conservative approach (standard of care) to regimen switching guided by resistance test result. This will also address the potential role of resistance testing in a clinical setting and how it may influence clinical management.

Conclusions. Both primary and acquired resistance are likely to increase in South Africa, as the antiretroviral roll-out programme matures. It will be critical to monitor the programme to determine in how far increasing numbers of people on ART, exposure to suboptimal PMTCT and late detection of treatment failure affect the resistance situation. This will enable informed decisions to be made on changes to the ART protocol. Clinical antiretroviral resistance monitoring is an area which will require further research and development to meet an increasing clinical demand and in order to monitor the long-term impact of HIV management algorithms within the national roll-out and PMTCT programmes.

Hypervirulent form of tuberculosis identified in Western Cape, SA

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Tuberculosis, caused by the bacilli *Mycobacterium tuberculosis*, is a major health problem worldwide. DNA fingerprinting has shown that the tuberculosis epidemic in South Africa is a composite of many different strains. These strains can be grouped according to DNA fingerprint similarity into genotype families which are in turn hypothesized to have unique properties. One of these genotype families has been designated as the Beijing family because it was first isolated in Beijing, China. Through comparative genomic analysis, it was possible to show in this study that the Beijing genotype originated from East Asia and was probably introduced into South Africa in the early 18th century. Phylogenetic analysis has provided new insight into the evolutionary history of the Beijing genotype family and has shown that this genotype family could be divided into 7 different sublineages. Isolates from one of these sublineage were found to be extremely successful in transmitting and causing disease in Cape Town, suggesting that these strains had evolved hypervirulent properties. However, comparative analysis showed that strains from this sublineage were not successful in East Asia, thereby suggesting an alternative scenario in which host population genetics may determine the ability of these strains to spread in the Cape Town population. We acknowledge that these contrasting conclusions can not be easily distinguished with the data available. However, the emergence of a sublineage of Beijing strains with increased pathogenicity may have important implications for the Tuberculosis Control Program. Early diagnosis and contact tracing will be essential to curb the spread of these strains. Furthermore, it will be important to ensure that future vaccines protect against these strains.

Read more ... Hanekom M., van der Spuy G.D., Streicher E., Ndabambi S.L., McEvoy C.R.E, Kidd M., Beyers N., Victor T.C., van Helden P.D., Warren R.M. A recently evolved sublineage of the *Mycobacterium tuberculosis* Beijing strain family was associated with an increased ability to spread and cause disease. [J Clin Microbiol.](#) 2007 May; 45(5):1483-90

Hanekom M., van der Spuy G.D., Gey van Pittius N.C., McEvoy C.R.E, Ndabambi S.L., Victor T.C., Hoal E. G., van Helden P.D., Warren R.M. Evidence that spread of *Mycobacterium tuberculosis* Beijing strains is human population dependent. [J Clin Microbiol.](#) 2007 Jul; 45(7):2263-6