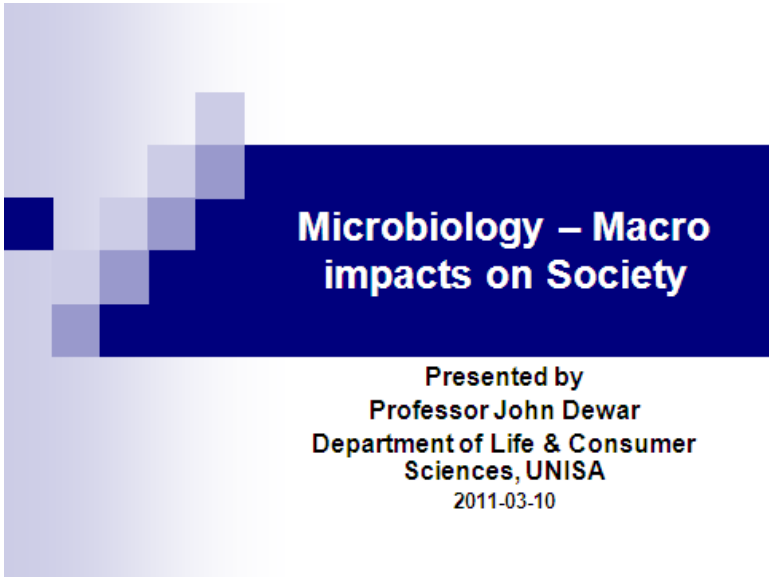


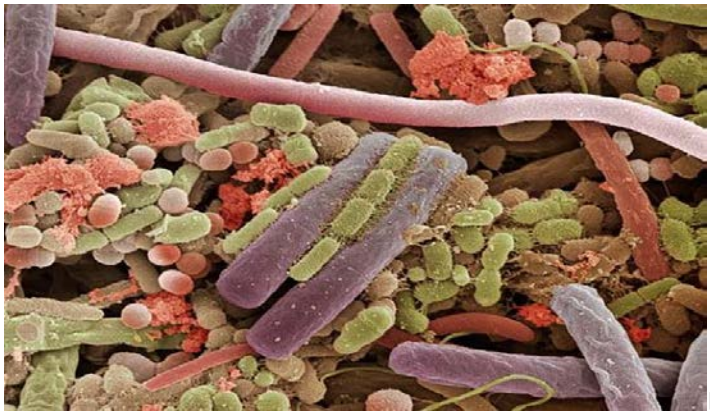
Professor John Dewar presented his inaugural lecture in the Senate Hall on the 10th March 2011. His lecture was entitled: "Microbiology – Macro impacts on Society". This lecture was oriented around the following themes: the UNISA Vision, Age and Icons, Mentors in Research, Future Research and the Unisa Science Hub. His lecture was as follows:

I feel privileged that Microbiology is as much a Social Science as it is a Life Science so that my experience can be applied to operationalise the Unisa vision, as being " …..towards the African University in the service of humanity". In practice, I hope to describe research activities that enjoy a similar broad focus and objective to UNISA's strategic projects that are to address factors that critically impact on South Africans. These include poverty and capacity development, HIV and AIDS, science and technology (including biomedical, agriculture & environmental research), open distance learning (ODL) and reflective research and responsible consumer citizenship. In all of these, skills transfer is a central theme.

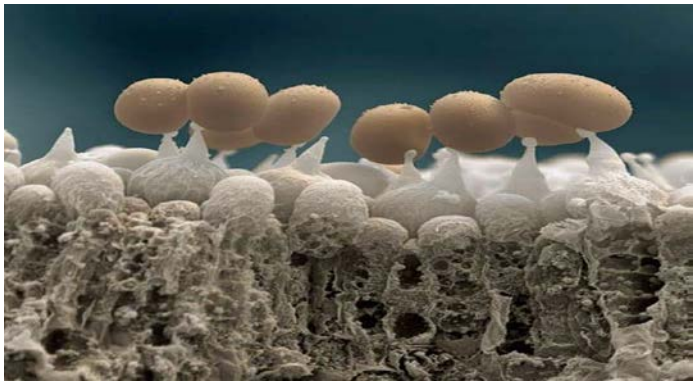
As an example of the relevance of the impact of microbiology on Society, I noted recently on a single page in an Eastern Cape newspaper (Eastern Province Herald, 22nd December 2010, page 16) the following: an Editorial: "Baby deaths demand urgent intervention", a lead article: "Metro must tackle pollution source and so clean up Swartkops River" and a cartoon comparing old, repackaged chickens to politicians.

While we are chuckling, may I also remind us of the links between microbiology and the practical science of biotechnology that seek to develop useful products by making use of new knowledge and techniques, particularly molecular biology techniques. Thus, a brief history of biotechnology may be depicted by the long-suffering 'Hagar the Horrible' who accepts a product of an ancient biotechnological process to help cure the symptoms of a cough!

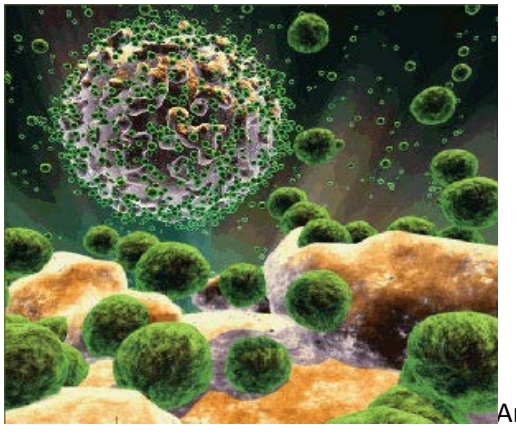
Before I start describing some of the impacts of microorganisms on society, may I take this opportunity of briefly outlining some of the fields of microbiology as depicted in the following beautiful (if artificially coloured) electron micrographs followed by an artist's impression of the environment faced by a human immunodeficiency virus:


Bacteria

The representation of bacteriology above shows various rounded as well as rod-like bacteria (so called, cocci and bacilli) that may, or may not, be pathogenic. Some of these bacteria may be responsible for throat and lung infections or gastroenteritis, all conditions of which are responsible for considerable morbidity, particularly within a third world context. It may be interesting to some of us that very often the cure for gastric ulcers simply involves a course of antibiotics to eradicate *Helicobacter pylori*, the spiral-shaped bacterium associated with the lining of the gut.


Fungal mycelium and spores

This representation of mycology shows some delicate spores perched on a fungal mycelium infrastructure. Most infections involving fungi are superficial and may include skin infections. However, many biotechnological products originate in research involving fungi including brewing and the development of many antibiotics such as penicillins, etc - we are all aware of the impacts such products have had on each of our lives and on society in general.


Artist's impression of HIV

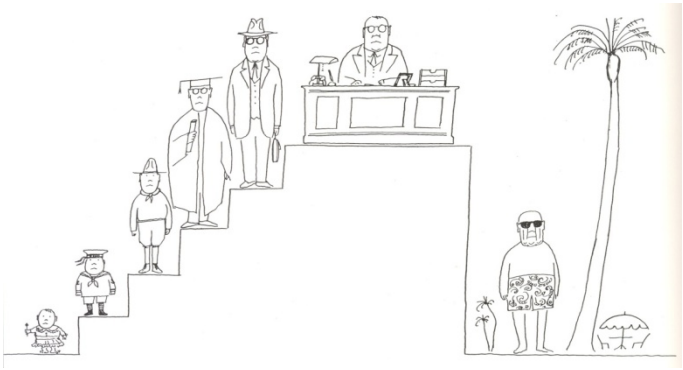
The rather 'Star Trek'-like depiction of HI viruses escaping from a human cell is very dramatic. As we know, infection and treatment of this virus was basically ignored in this country for many years and this has resulted in a massive burden not only on our HIV-infected population but also on the budgets and the normal activities of our healthcare services.

Having depicted, in very broad brush strokes, some of the practical and social aspects of microbiology, I would like to move on to some of the other themes in this lecture.

The first one upon which I would like to touch, involves age and ageing and the importance that experience and wisdom play in modern science. I can quite honestly say that I am not the youngest person presenting an inaugural lecture so I am intrigued as to what lies ahead…. . As a scientist, I naturally went to the literature to determine some features of age. I came across a beautiful (and, incidently, not very depressing) book called "The History of Old Age" filled with art work, photographs, quotations and diagrams. I enjoyed Cicero's opinion of old age:

'*Old age will only be respected if it fights for itself, maintains its rights, avoids dependence on anyone and asserts control over its own to its last breath.'*

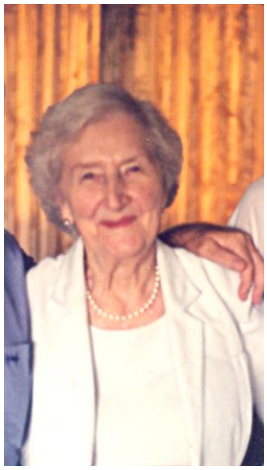
And of course, I enjoyed the various stages of academic development, perhaps leading eventually to the nurturing of mentors within an ODL environment!



More practically, I thought this photograph might presciently show me in a few decades time, helping to put some of the finishing touches to the Science Hub at the Unisa, Florida Campus!

On a more serious note, and as I move into another theme of mentors and icons, I would like, at the risk of severely embarrassing her, to introduce to you my mother, Dr Joan Dewar, who is in the audience. Next to her, and her namesake, is my lovely daughter, Joni. Before going into more of my mom's life

and experiences, I want to say, simply, that my father was a man of enormous intellect and humour and I miss him tremendously.



My mother grew up in Empangeni, Kwa-Zulu Natal, where she learnt to speak fluent, colloquial isiZulu. She completed a BSc (Botany) in 1939 and MB.BCh in 1945. She started a family before returning to medicine in 1960 where she trained at Livingstone Hospital and SAIMR (now NHLS) - so she has experience in the realities and challenges facing primary healthcare in this country. Having professional parents who worked very long hours indeed, and being the youngest of four, very active children, I feel that I had practical experience of ODL, often within a very challenging environment! My sibs actively put into practice survival of the fittest-type Darwinian theories, so we all quickly learnt to defend ourselves. Back to my mom: she started a medical practice (for 35 years) before moving to the Dora Nginza Clinic and Provincial Hospital. As a tribute to her, I wanted to end off by telling a story concerning her patients from the Dora Nginza Clinic. Now well into her 80's and because the Dora Nginza Clinic was around 30 kilometres from her home, my mother decided to move to Provincial Hospital OPD in the city itself. I very clearly remember long rows of the happiest-looking patients waiting outside my mother's consulting room, patients who had taken the effort to travel all the way into Port Elizabeth at considerable expense to consult with the "gogo" and were now catching up on the local gossip. This is what medicine should be doing, not only making people well but also making them happy. My mother retired from medicine aged 87. Well done, Ma, you are a star and an inspiration to us all!

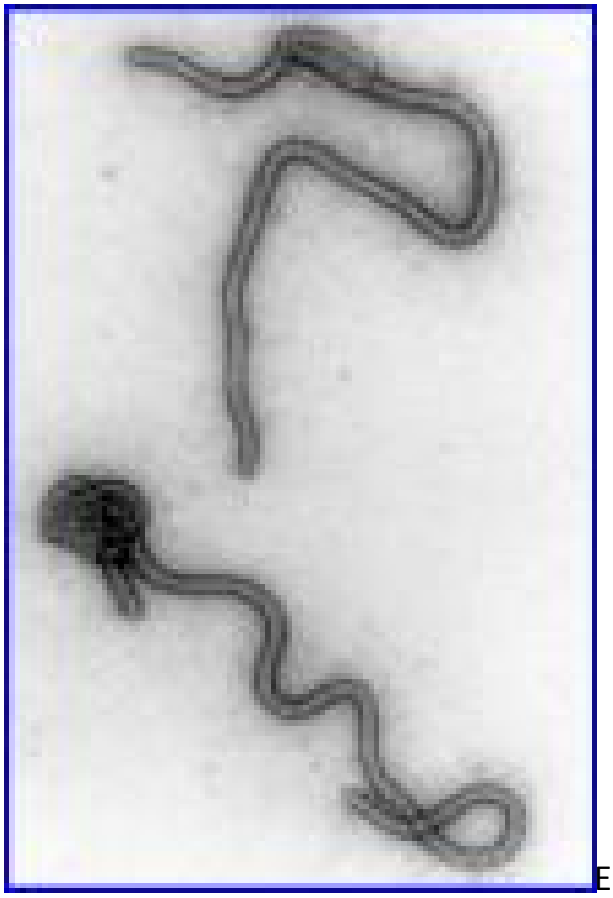
Microbiology is serious and requires serious people to face serious challenges. So at the risk of shocking us all……. a reality check…..

This is an image of a bird that died in an oil slick… and, oddly enough, is an introduction to some of the mentors and colleagues who have played such an important part in my academic career.

I obtained a BSc Honours degree in both Microbiology and Chemistry, an experience that required quite some recovery time! One of my Honours supervisors literally witnessed the grounding of the Torrey Canyon on the coast of Cornwall in 1967. He was appalled by the destruction of the environment and the response of the Wilson government which was to bomb the oil slick. So much so, that, when years later I was one of his students, there I was, scraping oily gravel from Grahamstown fuel station forecourts from which I isolated oil-degrading bacteria. My project eventually showed that a bacterium, a *Pseudomonas,* could be used to degrade all of the chemical components of crude oil except for the asphalt component. I sometimes wonder, with all the pot holes in our roads today, whether some of these bacteria managed to escape onto the roads to cause such trauma to our drivers..? In this respect, bioremediation, the use of microorganisms to degrade a pollutant, is currently being widely used. This technique was successfully used to clean up the Alaskan coast after the Exxon Valdez went aground and after reading the acid mine drainage Government Experts Report, I seriously think that we should explore the possibility of including bioremediation in the treatment of AMD.

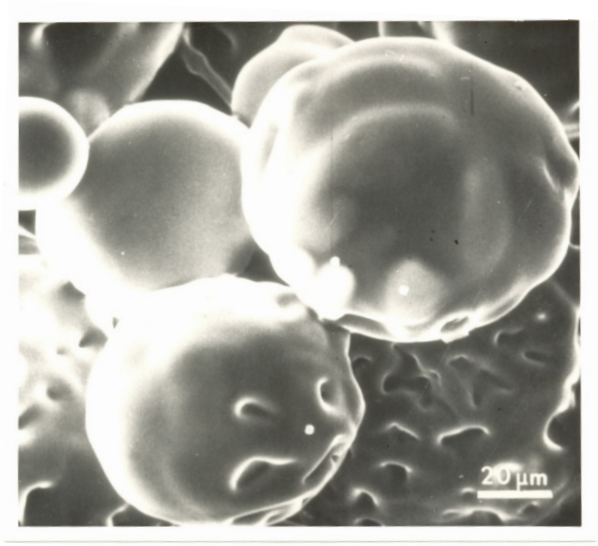
Acid mine drainage results from the metabolic activity of a group of bacteria, including *Thiobacillus ferrooxidans*, such that, in the presence of water, the oxidation of the sulphur component of pyrite rock, as found in our mines, leads to the production of sulphuric acid. Here on the Reef, rain water entering disused mines contributes to a rising level of this sulphuric acid so that, untreated, this AMD is estimated to start flooding our Johannesburg basements by March of 2013. Unfortunately, the AMD Report hasn't really emphasized the presence of radioactivity in this rising tide of AMD. However, we may become aware of radioactivity once our houses start glowing in the dark! Regarding water loss, its reuse and the ever reducing availability of potable water, we must hope that our politicians take cognizance of some of these simple facts of life so that they should disregard who is responsible for AMD and actually do something about this critical situation. It goes without saying that water is such an incredibly scarce commodity that it is not unrealistic to consider the possibility that wars will be fought in the future over access to drinking water!

On a slightly lighter note, I thought I would mention a few more bacteria, including *Bacteroidetes* and *Firmicutes*. It may just be possible to change our body shape were we to change the bacterial composition of our gut. Research has shown that individuals with a fuller figure may have mainly *Firmicutes* bacteria compared to the relative number of *Bacteroidetes* bacteria in their intestines. Something as fundamental (or as complicated) as our gut flora may impact on our quality of life resulting from obesity and the concommitant health sequelae such as diabetes, stress on joints, .. etc). A cartoon relating to one's figure reflects this……



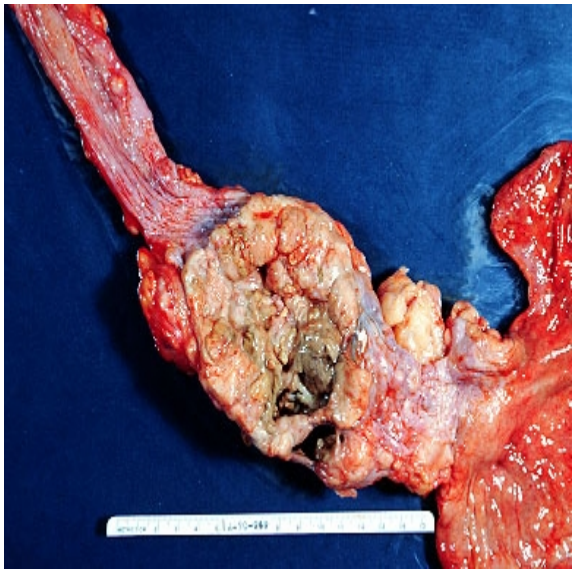
Ebola viruses

Following my Honours, I went into the field of virology, first while developing a virus vaccine formulation during my MSc and then into molecular virology during my PhD where I looked at various factors contributing to the development of oesophageal cancer, including infection with viruses such as human papillomavirus.



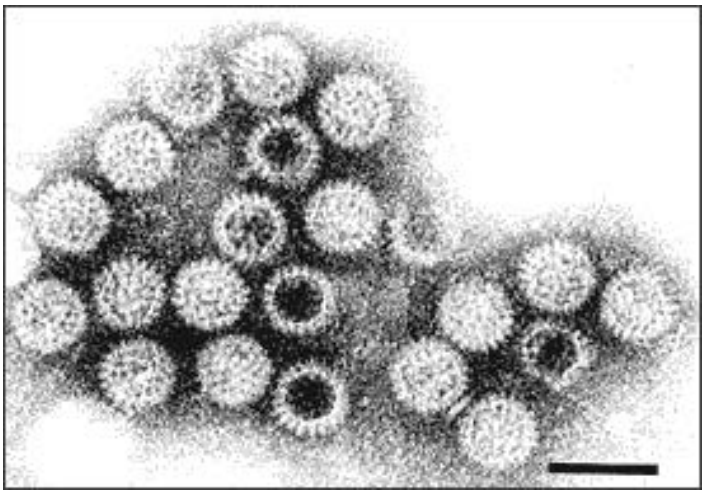
My boss for my MSc was Professor John Newman, who had performed research on foot-and-mouth disease virus and on poliomyelitis virus. Why I got into vaccine development was because in 1982, the Eastern Province Herald reported that some children in Gazankulu had received the oral poliomyelitis vaccine and had then shown signs of paralysis. This tragic report sensitized staff and students at Rhodes to the need for effective, safe vaccines. The basis of my research was an article by Lee *et al*., (1981) who proposed the encapsulation of hormones such as progesterone within serum albumin beads. We decided to replace the hormone component of the above bead formulation with virus as antigen, to develop a vaccine. This involves forming a cross-linked protein and antigen cage structure - the antigen is the protein that elicits a protective immune response – so that as the protein cage is degraded in the body, the antigen is gradually released to stimulate the immune system over an extended period of time. Note that Ethics committees were not very powerful 25 years ago! I worked on rabbits and mice for 2 years and was never required to submit an ethics application! Coming back to the present, as a reviewer of National Research Foundation research grant applications, I was interested to note that current researchers are showing an interest in macromolecular cross-linked structures for extended drug release.

For my PhD, I was fortunate to have Professor Jenny Alexander as my supervisor. A brilliant person who was the first to propose that infection with the Hepatitis B Virus was directly linked to the development of liver cancer. She was also convinced that infection with human papillomavirus followed by integration of HPV DNA into the target cell DNA, was associated with the development of oesophageal carcinoma. The oesophagus is a powerful and relatively inflexible tube so that any increase in cell number and mass causes a constriction of the lumen that eventually may block the oesophagus, as shown, rather disturbingly, in the photograph of a resected oesophagus.

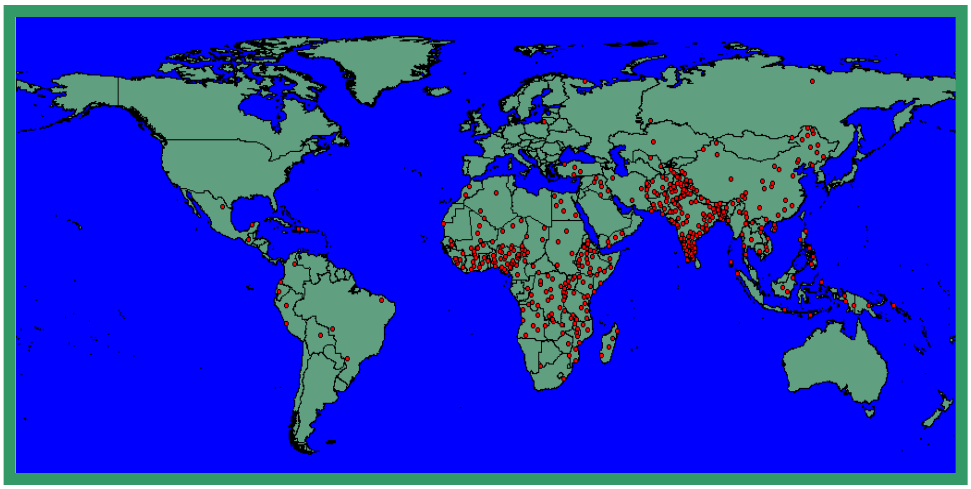


Analysis of the incidence of oesophageal carcinoma shows a geographical distribution limited to specific sites such as parts of northern China, the coast of the Caspian Sea, and here in sunny South Africa, in the, then, Transkei. In the Transkei, it was noted particularly in black males as a cancer with the highest incidence (at 36%) of all cancers. This could be a pan-African problem as the worldwide incidence of this

cancer has a rate of around 2 cases per 100 000 individuals, whereas an incidence rate of 58 cases per 100 000 men has been noted in Zimbabwe. Some of my PhD results obtained by PCR and flow cytometry indicated that, compared to a normal cell, a number of genetic changes had occurred in the oesophageal cancer cells. These included: an increased number of chromosomes (n=57 compared to the normal n=46), an inactivating mutation of the p53 gene (a type of genetic quality assurance agent), mutation within the N-acetyl transferase gene that resulted in altered activity of the encoded enzyme, activity of the telomerase gene, and the presence of human papillomavirus 18 sequences integrated into the DNA of cultured oesophageal cancer cells. Introduction of plasmid vectors expressing p53 into the oesophageal cancer cells induced specific, apoptotic oesophageal cancer cell death. This result turned out to be very specific for the cancer cells and may have implications regarding possible gene therapy treatment of OC. Compared to the graphic photograph of a resected oesophagus, it is nice to think that a cancer treatment regimen for OC might be as intrusive as simply gargling with recombinant DNA. While I was completing my PhD, I established a research collaboration with Dr Christine Gaillard (who is present in the audience tonight) at the Wits Medical School. This collaboration resulted in marvellous research and MSc student-training, particularly in the field of immunology.

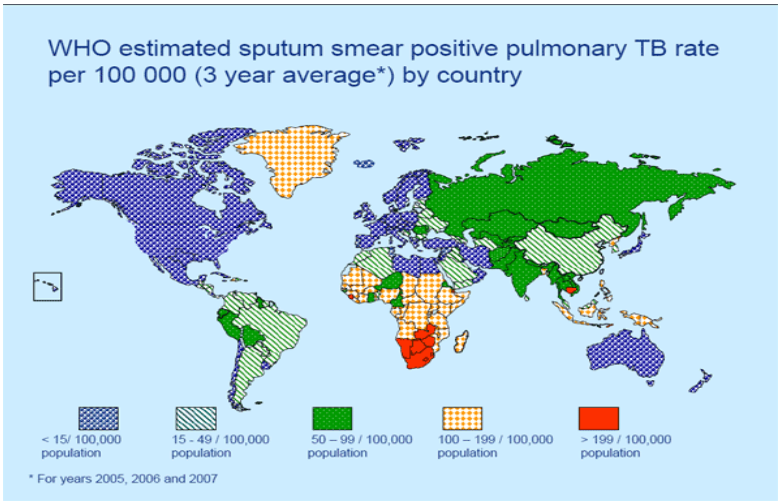


Following my PhD, I entered the rotavirus research environment where I was asked to direct a Medical Research Council (MRC) Research Unit, the MRC Diarrhoeal Pathogens Research Unit at the Medunsa campus. Rotavirus research very easily makes one become passionate to help the innocents and, thus, keen to go to work every day - this, particularly when one views the global distribution of rotavirus mortality that indicates that virtually all deaths associated with rotavirus infection occur within third world countries. The fact that these countries have a relatively reduced capacity to accurately determine the morbidity and mortality associated with rotavirus infection probably means that these figures, in all likelihood, are a (massive) underestimation.



Annually, rotavirus infection is responsible for around 650 000 deaths in children under the age of 5 years, and, as indicated, these deaths occur mainly in developing countries. In temperate climates, rotavirus infection shows an increased incidence in the winter months and, like influenza, rotavirus genotypes vary from year to year. I was privileged to be an investigator in rotavirus vaccine trials that were conducted in South Africa leading to the subsequent introduction in South Africa of a rotavirus vaccine in 2009.

More recently, I have started research into tuberculosis (TB), particularly regarding the development of multiple and extreme drug resistance (MDR and XDR) in these bacteria.



TB affects millions of people around the world and particularly in sub-Saharan Africa. UNISA, expanding into TB research, is an opportunity to make an impact on TB treatment (particularly regarding the incidence of antibiotic resistance in TB). It also allows us to establish research collaboration between UNISA and other research facilities such as those located within the Faculty of Health Sciences of the University of Witwatersrand.

I thought that I would start ending off my presentation by briefly looking at some topical issues.

I have just mentioned some of the challenges associated with the development of antibiotic resistance in TB and so we must be concerned when we hear dramatic reports such as: “The war against pestilence is over” (Surgeon-General, 1969) as opposed to just over 25 years later (in 1996), when the WHO director-general warned that “We are standing on the brink of a global crisis in infectious diseases. No country is safe from them”. It is obvious that increasing antibiotic resistance shown by microorganisms reflects as much on our poor antibiotic treatment regimens as it reflects on the magnificent survival strategies shown by these microorganisms. As such, it is incumbent on us not only to continue our antibiotic research and development but also to develop novel strategies to combat microbial infections. Perhaps, then, we should seriously think about alternative bacterial treatment modalities and one such is based on the use of bacteriophages – viruses that have specifically adapted to parasitise bacteria. Since the mid-twentieth century, bacteriophages, rather than antibiotics, have been used in poorer countries of the then Eastern Bloc, to successfully treat, particularly, surface wound infections involving antibiotic-resistant bacteria. We must consider funding and conducting research involving such treatment regimens.

I am not very optimistic that a vaccine will be developed to counter HIV infection. However, some optimism lies in the strategic initiative between UNISA and the CSIR involving bio-prospecting to isolate and assay medically active compounds from plants. Thus, we might well isolate compounds from plants that might be effective in treating HIV/AIDS as well as diseases such as TB and malaria.

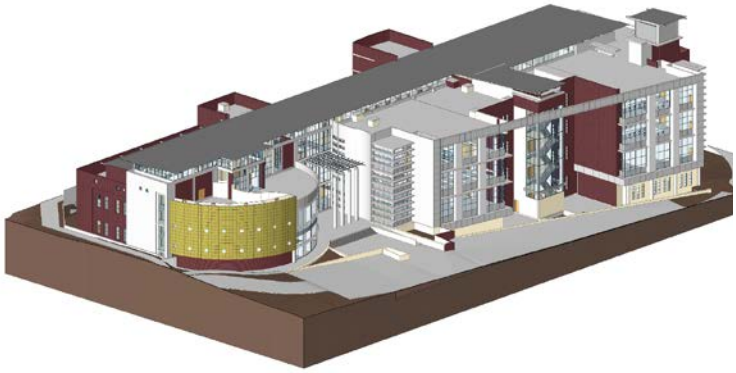
Regarding HIV treatment - with such a massive cohort of HIV +ve South Africans and with the massive logistics and price associated with antiretroviral therapy (ART), we need to ask fundamental questions such as: “When should we start antiretroviral therapy? Is the current therapy appropriate for a particular patient?” Currently the ART protocol involves determining a patient’s viral load and when that patient’s CD_4 count is below a threshold level, the patient is placed on ART, an expensive treatment regimen requiring extreme discipline and near perfect compliance with the treatment protocol. In addition, determining viral load and CD_4 count involves expensive equipment and reagents plus well-trained staff and, generally, across Africa relatively few laboratories have these assets. Moreover, research has shown that elevated serum urokinase plasminogen activator receptor (suPAR) levels are prognostic of a poor outcome in infectious diseases and, in the case of HIV, prognosis is proportional to suPAR titre and not to viral load or CD_4 count. Thus, HIV +ve patients may have a low viral load and a

high CD_4 count but still be extremely ill, and, incidentally, such patients show a high suPAR titre. Thus, in determining appropriate HIV treatment, it is important to note that there are WHO screening laboratories across Africa that have enzyme-linked immunosorbent assay (ELISA) equipment and competent staff who could titrate suPAR levels in HIV +ve blood sera. Because suPAR titration is ELISA-based and because such analyses may feasibly be used across Africa, we must question the protocols that demand sophisticated analyses associated with viral loads and CD_4 counts and, perhaps, we should consider alternative, more accessible (and perhaps more relevant) analyses to provide optimal treatment for our patients.

I would like to mention an African reality regarding applied microbiology. The WHO and an international pharmaceutical company successfully tested a vaccine and relatively recently met representatives of African Departments of Health to introduce a vaccination programme. Note that I mention no names. Linked to the vaccination programme was a 5 year subsidy that would be reduced by 20% each year so that the subsidy would fall away after five years. The response from these Health Department representatives was to confirm their acceptance of the introduction of the vaccination programme only while the WHO-subsidy applied and to then halt the vaccination programme once the subsidy period ended. This mercenary attitude was disappointing, to say the least.

UNISA has students, future leaders, all over Africa, who must champion appropriate technological advances in Africa and beyond. Such attitudinal and championing attitudes must be nurtured within Unisa students and also by developments within UNISA. One of these developments is the Science Hub at the Unisa, Florida campus. I believe this to be a fantastic investment in our continent's future and it is unfortunate that there has recently been bad copy in the press about the Science Hub, particularly as many Unisa undergraduate students have contacted me concerning the Science Hub as an incentive to complete their studies. We must make a success of research within the Hub and place Unisa on the research map as a serious contributor to socially relevant research within and without Africa. I leave you with an architect's view of one of the buildings in the Science Hub.

South view



I want to thank each of you, Vice Principal Academic and Research, the Executive Dean of CAES, the CoD of my Department of Life and Consumer Sciences and you, my family, friends and colleagues, for your attention and for giving me this opportunity to present my inaugural lecture. It is humbling for me to stand before such a talented audience.