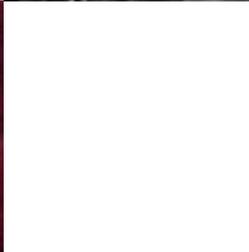




UCL

THE CHALLENGE OF TB: UCL'S CONTRIBUTION

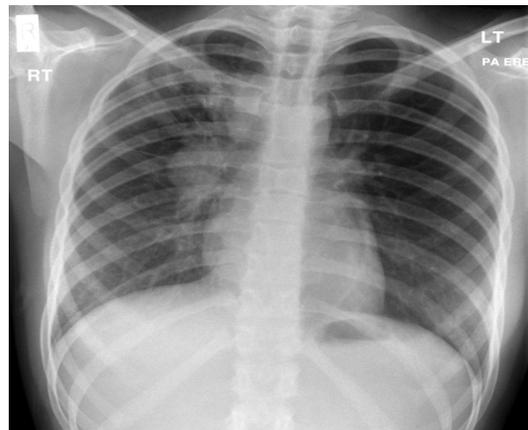


The Challenge of TB: UCL's contribution

On World TB day 2010 UCL's Institute for Global Health held an inaugural afternoon of presentations to mark 'The Challenge of TB: UCL's Contribution'. The program consisted of an exciting range of varied topics and speakers representing the multi-faceted nature of this disease and illustrating the multiple levels on which the battle against TB is being fought.

The afternoon was chaired by Dr Tim McHugh from the UCL Centre for Clinical Microbiology, which is a leader in the field of international microbiological research into TB. He introduced Dr Marc Lipman (UCL Medicine) who began his plenary presentation by marking events of the past year including the release of the film *Bright Star*, documenting Keat's last years prior to his death from TB, and the death of Sir John Crofton - one of the pioneers in TB treatment - who died in 2009 aged 97 years. Dr Lipman presented figures illustrating an increase in numbers of active TB cases across the UK by 5.5% in 2009, noting a particular issue with rates in London, which are the highest per population of any capital city in western Europe. This was taken up in Dr Andrew Hayward's (UCL Infection and Population Health) presentation about the overrepresentation of patients with TB in London of 'hard to reach populations' including those in prison, the homeless and drug users. Dr Hayward's department has just been awarded an NIHR program grant for the management and control for TB in hard to reach groups. He is also been representative on the NICE review group recently set up to provide guidelines for management of TB in hard to reach groups.

The role of imaging in TB diagnosis and management was covered in three presentations during the afternoon. Dr Charlotte Cash (Radiology, Royal Free Hospital) reviewed the role of imaging in the diagnosis of TB, talking about characteristic appearances, atypical presentations, and the role of imaging in obtaining tissue samples. Suzanne Bartington (MBBS Student, UCL Medical School) followed this by presenting audit findings from the Royal Free Hospital, examining compliance with NICE guidelines advocating chest X-Ray (CXR) for all with TB.



X-ray showing TB (Image: Dr Charlotte Cash, Radiology, Royal Free Hospital)

Later in the afternoon, Ben Irving (PhD Student, UCL Centre for Health Informatics and Multiprofessional Education) presented work on 'Automated analysis of the airways in CT scans for the modelling of TB'. This innovative project, in

conjunction with colleagues from Cape Town, SA, is looking to mathematics and physics to develop a screening tool to detect TB based on digital radiography. The process aims to analyse 3D CT images of airways of patients with TB to develop a statistical model of airway deformation that can be used to screen for TB. The 3D findings will later be applied to 2D radiography to develop the screening tool further.

Professor Stephen Gillespie (UCL Centre for Clinical Microbiology) presented a plenary session giving a history of TB treatment to the present day; through pre-drug therapy and the pivotal first testing of streptomycin, to combination drug trials, and then the eventual development of 6-month therapy. From there he discussed present developments in TB drug development and clinical trials, in particular the importance of collaboration illustrated by 2 major projects currently underway at UCL; REMoxTB study and PanaCEA consortium which both aim to contribute to capacity development of clinical trial sites to enable testing of the increasing number of TB active agents and thus speed the introduction of new treatments.

The afternoon's third plenary session was given by Dr. Carole Reeves (Wellcome Trust Centre for the History of Medicine at UCL). As an outreach historian, she gave a fascinating insight into life in a TB sanatorium from her collective history of Craig-y-Nos, South Wales. In operation from 1922, this TB Sanatorium for children and young women closed in 1959 with the introduction of the first antibiotics effective against TB. Her research began through

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work initiated by a previous patient, and rapidly expanded due to an overwhelming response to the Craig-y-Nos blog, resulting in over 150 oral histories and more than 1250 photographs. Patients recounted memories of their TB treatment; from the discomfort of having a gastric lavage, to sleeping outside on the balconies in the Welsh winters and waking under a tarpaulin heavy with snow. The social consequences of the disease were also highlighted, with many patients feeling ostracised and abandoned by families, friends, and no chance of future employment through fear of contamination. However, among these accounts were also many happy stories and photographs of the fun and friendships that were made between the children and women, several of whom have been reunited decades later as a result of the project. A book documenting this history has recently been published.

Dr Helen Donoghue (UCL Centre for Clinical Microbiology) highlighted TB history of a different kind. She presented her work on the detection of ancient TB from the Neolithic period, in bones from Egypt and mummified remains discovered in a Hungarian crypt. Evidence of previous TB infection can be seen directly from skeletal lesions in the bones. However, these can be confused with other illnesses and Dr Donoghue's work has focussed on the definitive detection of TB by identifying markers of the organisms itself. Her work has shown TB bacteria present in calcified lung lesions using standard staining methods, but more importantly has developed techniques to detect TB DNA, as well as TB proteins and cell wall lipids, from ancient material. These techniques confirmed the earliest

known case of human TB over 9000 years ago, and the invention of the field of 'paleo-microbiology'. By comparing this ancient DNA with TB from today, Dr Donoghue's group have been able to study the evolutionary history of TB and its co-evolution with humans, corresponding with a switch from the hunter-gather lifestyle to larger settled communities and the introduction of agriculture and domestication.



Calcified pleura in ancient Egyptian mummy (Image: Dr Helen Donoghue, UCL Infection)

Using similar molecular tools in modern diagnosis, Dr Clare Green (UCL Centre for Clinical Microbiology) presented her data on the use of urine as a diagnostic target for pulmonary TB. She described the small, cell free nucleic acids, known as transrenal DNA, that can be detected in urine of infected individuals. Previous studies have shown huge variability on the sensitivity of this assay of the detection of TB, and Dr Green's work has examined factors that might influence this variation - such as the patient group, sample preparation and the assay design - in order to try to optimise this technique as a clinical tool. Prof. Brian Henderson (UCL Eastman Dental Institute) talked about the role of heat shock proteins in the pathogenesis of

tuberculosis. These molecular chaperones are known virulence factors in a range of pathogens and the work presented suggested a possible role in granuloma inflammation in TB. Professor Nick Keep (Biological Sciences, Birkbeck) explored further the molecular pathogenesis of TB and described his work on TB resuscitation promoting factors. These bacterial 'cytokines' have been shown to be important for waking up dormant M.tb.

The day was rounded up by the final plenary speaker, Professor Graham Rook (UCL Centre for Clinical Microbiology) who gave a broad overview of TB immunology and the potential for TB immunotherapy as a countermeasure to the long and complex courses of antibiotic treatment. He explained the careful balance between cytokines that are thought to be important for driving the progression or resolution of latent TB infection. Promising data for the potential of manipulating these cytokine responses to improve the outcome of TB infection was described in mouse models and progress is also being made to investigate these findings in humans, with discussions ongoing with pharmaceutical companies about possible roll out to full clinical studies. Two other new vaccines, the Hsp-65 DNA vaccine and vaccination with the saprophytic mycobacterium *M. vaccae*, were also discussed. The Hsp-65 vaccine is moving into human studies in Brazil and Japan, whilst a recent study of *M. vaccae* vaccination in BCG-primed HIV positive patients with TB showed promising results. Professor Rook discussed the possibility of targeting those patients that are failing treatment for XDR TB with vaccine treatments.



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Improving awareness of Tuberculosis

The presentations in this meeting have illustrated that TB is not only a disease of the past and present but, if we do not meet the challenge, it will be very much a disease of the future. The meeting was open to all of UCL and UCL Partners and a wide range of undergraduate and postgraduate students attended; it will be these future opinion formers and leaders that will be critical in overcoming the challenge of TB.

With this aim in mind we extended the invitation to attend our event to 6th Form students from Burntwood Foundation School, Wandsworth. These students found the meeting 'informative and interesting' and Isabella Keller commented that 'Learning how different social groups are affected by TB gave me a new insight into treatment plans and application'.

To watch all the presentations given at this Institute for Global Health event please visit www.ucl.ac.uk/global-health/events/previous or download and watch via UCL on i-tunes U.

Report by Dr Kasha Singh and Dr Anna Bateson,
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The cross-fertilisation of UCL's expertise in global health is co-ordinated through the UCL Institute for Global Health. The institute is developing a university-wide agenda leading to strategies, programmes, research and teaching to bring our combined expertise to bear on the grand challenge of global health. To find out more please visit www.ucl.ac.uk/global-health