

Infectious Diseases & Immunity News

Biannual newsletter from the Department of Infectious Diseases & Immunity at the Hammersmith Campus of Imperial College London



Overall it's been another good year for the Department. However, as many of you know, there have been occasional bumpy patches. We continue to grow in terms of personnel, partly as a result of some very large grants. The Centre for Infection Prevention and Management (CIPM) funded by £5 million from the UKCRC got off the ground this year and we've welcomed a range of talented people from PhD students to clinical researchers. Inside, Danny Altmann reveals how to relieve the NIH of \$5 million, following what can only be described as a highly successful application!

Many of you will be aware of the restructuring process that went on at Imperial College London and although there were many concerns, in the end we lost one administrative post. Many thanks to those who kept working hard even when their jobs appeared to be at risk. The final part of the jigsaw not yet in place is a new laboratory manager, but this is in hand and hopefully a good person will be in place early in 2010.

Teaching continues to be a major strength of the Department at both undergraduate and post-graduate level. There has been a new medical student introductory firm on the wards and we are contributing to the new graduate school of medicine in diverse ways. The MSc courses go from strength to strength and Mick Jones must be congratulated on recruiting over 30 people to his MSc which is probably a College record.

It never ceases to delight me that for each Newsletter there is another list of talented people who have obtained awards. Look inside and congratulate them. Every year in addition to welcoming

new members to the Department, we say farewell to others. I particularly wish to thank David Moore who has been an outstanding contributor to the Department for most of this decade working mainly not in W12, but in Lima, Peru.

As to the future, we shall continue the integration between clinical and academic medicine that has always been a central feature of our work well before the AHSC came into existence. In particular, I am hoping we shall increase the number of patients being involved in clinical trials run from the Department as well as continuing with our work on human pathophysiology of infection. For more senior staff, 2010 represents a grant gaining opportunity ahead of any tightening of belts that may follow from the banking crisis.

I am keen to stress that every member of the Department has an important role to play in our development and if any of you have ideas or suggestions, please do pop in and share them even if they are only half-formed.

Season's greetings and best wishes for 2010!

Jon

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With MRC grant panel award levels currently withering in successive grant rounds from 23 to 15 to 11%, it's critical to keep looking to additional funding openings in Europe and the U.S.

However, at a time when

U.S scientists are complaining of RO1 NIH application success rates dropping below the 20% level (read Nature 457 (5) 650 if you want a truly depressing experience) it probably takes a lot of gall (the etymologically accurate term is chutzpah) to fund a UK lab through US NIH funding. Having been generously funded for the past 5 years by the NIH-NIAID Immune Epitope Database (IEDB), we put considerable effort into a new application to them when a follow-up call

'As a non-US lab we felt we had to bid high'

was announced earlier this year. We recently heard that there were six successful applications, ours being one of them.

As a non-US lab, we felt we had to bid high, and offered a comprehensive approach to analysis of two pathogens on the A-C list, anthrax and plague. This ranged from CD4 T cell analysis in protein-immunised or infected panels of HLA transgenic mice, to panels of T cell hybridomas, HLA binding studies and analysis of human vaccinees and convalescent patients. In order to do this, we had to assemble a diverse array of collaborators and expertise in Newcastle, Maryland, France and Porton Down. At our end, terrific people worked on the project – Steff Ascough, Louise Kim, Karen Chu and Beckie Ingram. The work has gone very well and among the discoveries, Beckie found during her analysis of Turkish farmers who had recovered from cutaneous an-

thrax that far from the expected immune paralysis, they showed massive and presumably protective, immune memory to some of the anthrax toxins.

The new programme of work will be on *Burkholderia pseudomallei*, the causative agent in melioidosis. Not a pressing clinical problem in East Acton, but the major cause of hospital and ICU admission for bacterial sepsis in Northern Thailand, stretching into Myanmar (Burma), Cambodia, Laos and Northern Australia. Sepsis from



Exposure to soil-dwelling *B. pseudomallei* in rice paddies

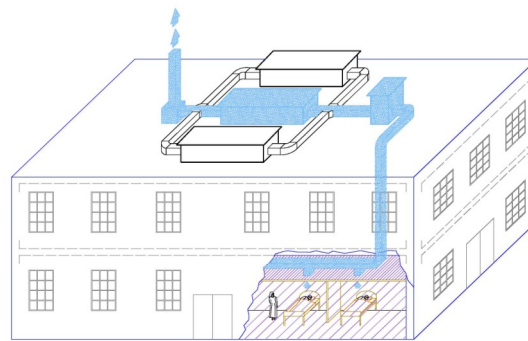
B. pseudomallei has a 50% mortality. I had no experience with it and no publication track-record, so what on earth made us build a multi-million dollar grant application around it? Lots of things: it has a fascinating, challenging spectrum of pathogenesis – why is it that in a setting where all are exposed to spores, some will remain seronegative, some will seroconvert without any clinical signs, some will suffer localized infections and others will become septic. One of the mysteries in the field comes from case reports of World War II POWs and Vietnam vets who were exposed and then showed disease reactivations up to 65 years later. Lots of great questions for an infection where there's no vaccine and not even a clear consensus on what should be the correct target for a vaccine in this disease. I was lucky in being able to assemble a team with considerably greater melioidosis credentials than myself (as you'll have gathered, not hard to surpass). Key among these were

Karen Chu, Greg Bancroft, and John Robinson along with Gan Lertmemongkolchai in Khon Kaen, Thailand.

So, what does this mean, if anything, about how to go about putting forward large NIH applications? Clearly my experience has been good and I'd advise signing up for NIAID notifications of new funding calls. The applications are a vast amount of work and always seem to involve long, through the night sessions, not just on the science, but the legalities of the supporting documentation. The quote about "two nations divided by a common language" never feels truer than when its 3am on the final day before submission and you're trying to decipher a form about whether your business has evidence of offering equal opportunities to Hispanic and Native American minorities. We have to be wise to, but not unduly daunted by, the clause that says funding will only go outside the US if there is evidence that this offers expertise that cannot be offered by US investigators. I don't for a moment suppose that the Altmann lab offers research opportunities unmatched by the 200m inhabitants of the US. However, the evidence seems to be that if you can get a foot in the door and establish some kind of reputation for delivering an ambitious package of work, they're prepared to listen.

Rob Escombe explains about a new way of dealing with airborne TB transmission

Airborne TB transmission in health care settings is a major public health problem, especially in today's era of epidemic HIV and drug-resistant TB. Prevention is based on a three-tiered approach: administrative controls to ensure prompt diagnosis, isolation and initiation of effective treatment; environmental controls to reduce the airborne concentration of infectious droplet nuclei; and personal respiratory protection. Our group in Peru looked at natural ventilation for preventing airborne transmission (*PLoS Med.* 2007;4:e68) but this is climate dependent. In parallel we studied upper-room ultraviolet (UV) light for sterilizing hospital air and reducing TB transmission. We knocked down the original guinea pig air sampling facility on the roof of a TB-HIV ward in Lima (where guinea pigs breathe the air directly exhausted from patient rooms) and built a bigger one, with multiple exposure chambers.



Schematic of guinea pig air sampling facility on roof of TB-HIV ward fitted with UV lights

The ward was remodelled into isolation rooms fitted with shielded UV lights, which flood the upper room with high intensity UV light, whilst the lower part of the room remains safe for patients and health care workers. Infectious droplets produced by coughing patients are sterilized on passing through the UV field, facilitated by small fans for room air mixing. One group of guinea pigs breathed ward air on alternate days with the UV lights switched on, and another group with the UV lights off. We compared TB rates in the guinea pigs after 535 days, and found a ~70% reduction in TB transmission. This is the first demonstration of the efficacy of upper-room UV lights for preventing TB transmission in a clinical setting and providing an evidence base for infection control guidelines (*PLoS Med.* 2009; 6:e43).

This relatively low-cost, low-tech, and low maintenance intervention provides an important tool for TB infection control, urgently needed in the overcrowded health care settings of the developing world where TB and HIV are rife.

Eimear Brannigan explains how management of HCAI demands a multi-disciplinary approach to provide effective care for patients and the prevention of future cases.

Management of healthcare-associated infection demands a multi-disciplinary team approach combining infection prevention and control expertise, clinical judgement and therapeutic decision-making, and a reflective approach to identify preventive opportunities for future patients.

Management of *Clostridium difficile* exemplifies the benefits of this approach, currently being promoted across the Trust. Each individual case requires that simple measures are implemented well. These include early recognition of infectious diarrhoea, timely isolation to limit the transmission of *C. difficile* spores to other patients, and attention to detail regarding antibiotic exposure of all patients.

‘Each individual case requires that simple measures are implemented well.’

In addition, fluid and electrolyte replacement, and early administration of the appropriate treatment agent are important in achieving the best outcome for each patient. Oral vancomycin has been shown to be more effective than oral metronidazole in severe *C. difficile* infection (CDI), but adjuvant strategies including intravenous immunoglobulin have been used in severe cases. Oral metronidazole alone is effective in mild disease. These multiple elements must form part of the management pathway for cases of CDI as they arise and all staff involved in patient care need to be aware of this inter-connected pathway, in order to minimise risk to others, and to prevent the occurrence of a period of increased incidence of CDI.

Learning from previous cases has identified areas for improvements in clinical practice and

interdisciplinary working. Getting the basics right is central, namely that clinical staff identify that a patient has diarrhoea, and recognise that an infectious cause is possible, and communicate with laboratory colleagues effectively about suitable diagnostic samples, appropriate tests, and accessing results.

Direct communication from the microbiology laboratory often provides as initial opportunity



for clinical case management recommendations, followed up by the infection prevention and control team which supports ward staff in case management, early isolation of cases, and ensuring they have the skills and facilities to implement effective control of potential transmission. Optimal additional management may require collaboration between the infection team, gastroenterologist, surgeon, pharmacist and dietician. One of our major roles has been in raising awareness among all medical staff of how to identify severe CDI, which often warrant an early surgical opinion and intervention.

During the autumn and winter seasons, the infection control messages relating to CDI prevention will also apply to prevention of transmission of norovirus and influenza, both already affecting the Trust in numbers; namely recognition, isolation, attention to hand hygiene and appropriate personal protective equipment.

EDUCATION

Mick Jones was appointed to the role of College Tutor earlier this year and has particular responsibility for students based on the Hammersmith Campus



Earlier this year, I joined a small group of fellow academics at Imperial College and was appointed as a College Tutor.

Although students, whether undergraduate, postgraduate or PhD, will still be allocated a personal tutor, departmental tutor or a supervisor who should still be the first point of contact when they require advice or support, in some cases this may not be appropriate or there may be a conflict of interests. This is where my role comes into play and students can speak to myself or one of the other four College Tutors who act in a similar capacity within the college.

All students have confidential access, independent of department or division, to College Tutors to discuss any academic issues, pastoral care and/or discipline within the College. This means that we are available at short notice to respond to

student enquiries. Given the increase in student numbers at Hammersmith, both undergraduate and postgraduate, it is extremely important that students know there is someone on site they can contact.

Luckily for most of my “clients” so far I have been able to help and sort out their problems. Mainly this has been a result of confidential discussions with the other College Tutors and knowing where to go for advice and/or knowing where to point the student. College has a remarkable student welfare and support system).

We also have a role in student discipline, with any student fines going to the College Hardship Fund. This is an experience I have yet to undergo.

Student welfare & support

- www3.imperial.ac.uk/students/colleetutors).
- www3.imperial.ac.uk/students/welfareandadvice

Tracey Norris brings us up to date with the department's Health & Safety news

Important changes are underway within the Faculty of Medicine and as a consequence the safety management system for ID&I will also change. After the 1st January, I will no longer be divisional safety advisor; a new campus safety advisor will be responsible for the Hammersmith Site; and Danny Altman will take over as departmental safety coordinator unit a laboratory manager is appointed.

The introduction of “The Biological Agents and Genetically Modified Organisms (Contained Use) Regulations” is due to be implemented in March 2010. The new regulations will cover deliberate work with wild type pathogens (human and

animal), and all GMOs replacing current COSHH, SAPO and GMO(CU) regulations. As an important consequence of this enforcing authorities are implementing fully cost recovery and charges for notification are likely to increase dramatically for deliberate work with wild type hazard group 2 and 3 pathogens. You should therefore submit any notifications quickly before the changes are implemented!



EDUCATION



Susan Farrell, Head of Education for CIPM, has responsibility for the Infection Seminars and various education initiatives within the department. Here she talks about the education programme.

The MSc Infection Prevention for Pharmacists started in October with 11 pharmacists enrolled on the

course, which is our highest intake to date. All the modules are being advertised as stand-alone courses and there will be a number of single study days as well.



Following last year's success, there are plans to run a third *Infectious Disease Update for Clinicians* course in March. This is a 2-day course and covers HCAI, Surgical Site Infections and Viral Infections.

Currently in the development stages is a new MSc course for nursing and/or management staff and a short course for non-medical prescribers. It is intended that CIPM's research and findings will contribute to the design of these (and other) courses. CIPM's ongoing research will allow education programmes to be monitored and designed to guarantee that they address the most relevant issues and teach staff how to deal with problems in the most effective way.

The Clinical Academic Infection Seminars continue to take place every Tuesday (12.30 – 1.30pm) and a new monthly seminar series has just started to report progress with the CIPM – International Health Management Research Collaborative.



The Centre for Infection Prevention & Management (CIPM) was awarded a £5m research grant and has created many education opportunities within the Department

The UK-CRC-funded Centre for Infection Prevention and Management (CIPM) is co-directed by Jon Friedland and Alison Holmes and is tackling the issue of healthcare associated infection via a multidisciplinary approach. This includes organisational research, social marketing, behavioural change, epidemiology, laboratory-based programmes and education.

The initiative, funded for 5 years, has created 13 new posts and 7 studentships. The multi-disciplinary approach of the Centre means it brings together many different Departments and Divisions in the College. Within the Faculty of Medicine these groups are; the Department of Infectious Diseases and Immunity and the Department of Experimental Medicine and Toxicology, within the Division of Investigative Science and the department of Primary Care and Social Medicine in the Division of Epidemiology, Public Health and Primary Care. The Centre also works with members of the Business School and the Cell & Molecular Biology Department in the Faculty of Life Sciences. It also brings together a number of organisations in collaboration with Imperial College London, including Imperial College Healthcare NHS Trust and the Health Protection Agency.

John Humphrey Seminar Series continues to thrive - attracting many prestigious speakers from around the country

The 2010 Immunology & Infectious Diseases programme continues every Thursday between 1-2pm

<p><u>14th January 2010</u></p> <p>Targeting regulatory T cells in rheumatoid arthritis</p> <p>Prof. Michael Ehrenstein, Professor of Rheumatology, UCL</p>	<p><u>18th February 2010</u></p> <p>Lysosomal proteases & their cystatin regulators in the immune response</p> <p>Colin Watts, College of Life Sciences, University of Dundee</p>	<p><u>15th April 2010</u></p> <p>Complement: Tipping the balance between successful host defence and autoimmunity</p> <p>Claudia Kemper, Department of Nephrology & Transplantation, King's College London</p>	<p><u>13th May 2010</u></p> <p>The roles for the D6 chemokine scavenger in innate and adaptive immunity</p> <p>Gerry Graham, Glasgow Biomedical Research Centre University of Glasgow</p>
<p><u>28th January 2010</u></p> <p>Pathogenesis of retro-viral infection: lessons from the mouse</p> <p>George Kassiotis, National Institute for Medical Research</p>	<p><u>4th March 2010</u></p> <p>T Cell inducing vaccines: Malaria, flu and more</p> <p>Adrian Hill, Director, The Jenner Institute</p>	<p><u>22nd April 2010</u></p> <p>Regulation of B cell development & Function by RNA binding proteins</p> <p>Martin Turner, Biotechnology & Biological Sciences Research Council, BBSRC</p>	<p><u>27th May 2010</u></p> <p>Life and death of a T cell</p> <p>Peter Krammer, Head of Tumorimmunology, German Cancer Research Centre</p>
<p><u>4th February 2010</u></p> <p>The function of integrins on immune cells: in sickness and in health</p> <p>Nancy Hogg, Cancer Research UK</p>	<p><u>11th March 2010</u></p> <p>The Molecular Basis of Lymphoid Stress Surveillance of Dysregulated Tissues</p> <p>Adrian Hayday, Peter Gorer Department of Immunobiology, King's College London *</p>	<p><u>29th April 2010</u></p> <p>Dissecting the cellular cytokine network</p> <p>Prof Werner Muller, Faculty of Life Sciences, Manchester University</p>	<p><u>10th June 2010</u></p> <p>TBC</p> <p>Moria Whyte, Academic Unit of Respiratory Medicine, The Medical School Sheffield University</p>
<p><u>11th February 2010</u></p> <p>Focusing on the Achilles heel of HIV-1</p> <p>Tomas Hanke, The Weatherall Institute of Molecular Medicine</p>	<p><u>18th March 2010</u></p> <p>IKK/NF-kappaB signalling in inflammation and cancer</p> <p>Manolis Pasparakis, Institute for Genetics, University of Cologne</p>	<p><u>6th May 2010</u></p> <p>CD4+T cell responses in heliobacter-induced intestinal inflammation</p> <p>Marika Kullberg, Centre for Immunology & Infection University of York</p>	<p><u>24th June 2010</u></p> <p>TBC</p> <p>Antal Rot, Birmingham University</p>

***PLEASE NOTE THAT THIS SEMINAR WILL TAKE PLACE BETWEEN 12.30—1.30pm**

Despite the wrench of leaving Peru, **David Moores** is looking forward to the challenge his new appointment brings and his continuing collaboration with research at Imperial

After seven years living and working in Lima, Peru my family and I returned to the UK in late August in time for my three children to start the school year. A simple sentence that disguises an extraordinary transition in professional and domestic life.

Arriving in Peru back in 2002 was highly challenging for all of us, not least because we arrived so hopelessly linguistically underprepared (vital lesson number 2 and a mistake never repeated for subsequent student visitors). In contrast, arriving back in England though initially somewhat alienating, was greatly softened by the extraordinary autumnal weather reminding us of the rich seasonality that we'd been missing in the coastal desert (we previously returned to the UK after 2 years in South Africa in the middle of a very wet winter - this was vital lesson #1 harshly learnt).

'Professionally, the work of my group continues, albeit with a rather more remote hand on the tiller'

But departing Peru was altogether something else - a masterclass in administrative carnage (we're still the reluctant owners of two vehicles in Lima) and a surprisingly painful domestic wrench for all. Professionally, the work of my group continues, albeit with a rather more remote hand on the tiller. Skype video conference calls efficiently shrink the distance and keep the engine ticking over but also consume the evenings, so some sort of improved balance still needs to be found.

And what of work in the UK? After seven years immersed in full-time research in a developing country the transition home (which had been driven entirely by domestic not professional considerations) was always going to be an interesting journey and I was decidedly uncertain about how I would want my

working week to look. When the opportunity arose to run the Diploma in Tropical Medicine and Hygiene at LSHTM and do clinical work at the Hospital for Tropical Diseases, with space for continuing research in the remaining time I was torn between a strong sense of loyalty to my friend and mentor over the past decade, Jon Friedland, and an enthusiasm to embrace a new career direction. Suffice to say that my gratitude to Jon for his wise counsel and good grace during what could have been distinctly awkward dis-



Martin Chambi

"Field work draws on a multidisciplinary team and an array of different headgear: Fiesta of the Guardia Civil, Sacsayhuaman, Cuzco, 1930"

cussions is huge and though I'm sad to be leaving the Department, I'm excited by the challenges ahead and I look forward to maintaining genuinely collaborative interaction particularly with the TB group.



A shanty town in Lima, Peru

CONGRATULATIONS: Staff, students and major grant successes

DOCTORATES:

- Tracey Pollard & Aceel Al-Anizi

PROMOTIONS

- **Alison Holmes** promoted to Professor in Infectious Diseases
- **Mick Jones** promoted to a Reader

PRIZES

- **Rob Escombe** awarded the **The Union Scientific Prize at the International Union Against TB & Lung Disease** and the **British Infection Society Barnett Christie Lecture**
- **Prathiba Kurupati & Claire Turner**, the ICAAC/ASM Pathogenesis award
- **Karina Corward**, 1st Prize for her presentation at the Royal Society of Tropical Medicine and Hygiene Research in Progress Meeting

GRANT SUCCESSES

- NIH-NIAID awarded \$5.1M to **Danny Altmann** 'T cell epitopes from Burkholderia pseudomallei'
- BBSRC awarded £750K to **Altmann, Boyton & Wiles**

'Multicoloured bimodality biophotonic imaging for analysis of immune cell differentiation'

- Wellcome awarded £297,230 to the **Altmann** lab HLA-C, killer immunoglobulin-like receptors & natural killer cells in multiple sclerosis'
- MRC/A*STAR awarded £337,487 to **Altmann & Rotzschke**, Cellular and transcriptomic analysis of regulatory T cells in streptococcal infection
- MRC awarded £211,617 to **Friedland**, 'The role of membrane-type matrix metalloproteinases in the pathogenesis of tuberculosis'
- Wellcome Trust awarded £120,258 to **S Sriskandan** for a studentship
- Collaborative grant with Cfl awarded to **Sriskandan and Turner**



Rob Escombe being awarded the Union Scientific prize at the Union World Conference in Cancun



NAME: Caroline Renaud

ROLE: Departmental Secretary

WHEN I WORK: I work 3 days a week, my days of work are Monday, Wednesday and Thursday.

MAIN RESPONSIBILITIES: I organise job advertisements for the department and deal

with the induction of new staff. I also organise new contracts and contract extensions that may be required and I set up bursaries for students.

I also have Finance responsibilities which include overseeing Departmental accounts and Grant accounts (except Danny Altmann's, Louise looks after these). I keep PIs and Jon up-to-date about each account and investigate any queries that may arise. I shuffle money between accounts (which sounds dodgy but actually it's charging monies to

the correct account). I'm also involved in the grant side of things and assist with the financial responsibilities such as costing for staff and consumables. During the lifetime of a grant I keep the PIs informed about how much they have left to spend and advise as and when monies begin to run short or when the grant is due to come to an end. Of course, there are also lots of other bits and pieces that emerge in the everyday life of this busy department.

THE THING I ENJOY MOST ABOUT MY JOB: I like the variety of my job

HOW I SPEND THE REST OF MY WEEK: The remainder of my time is spent working as a Dog Behaviourist. This involves helping dog owners with a variety of problems that their pet may develop, such as separation anxiety (some dogs get very distressed when their owner leaves the house), aggressive behaviour, chewing furniture, chasing cars etc. I also work as a tutor for the Open University in Medical Imaging.

Selected recent publications from the Department of Infectious Diseases & Immunity

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