

# Infectious Diseases & Immunity News

Issue No 7 spring/summer 2007

The newsletter from the Department of Infectious Diseases & Immunity at the Hammersmith campus of Imperial College, London

It has been another successful 6 months for our Department. Everyone will be aware that we are now in temporary accommodation while our Department is being entirely re-built. It will be great to be in new facilities which will be fit for purpose even though it is cramped at the moment. This is particularly so because the number of researchers in the department is pleasingly on the increase. It is a great pleasure to welcome the new post-doctoral scientists, clinical training fellows and students to the department. This all reflects healthy grant income that is a result of hard work by PIs. At the output end, publication output remains plentiful and of high quality with recent papers in *The New England Journal of Medicine*, *Nature Medicine*, and *PLoS Medicine* all testifying to this.

We have been spreading the word and it appears that a lot of people want to hear it. As you will read inside, the Departmental annual "Update in Infectious Diseases for Physicians & Scientists" was oversubscribed and had a waiting list of 15 people.

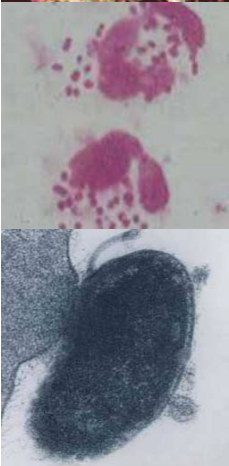
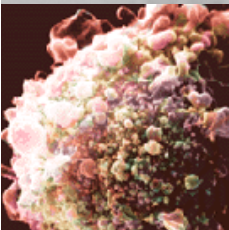
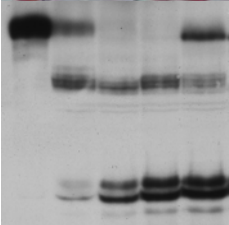
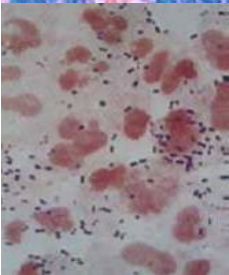
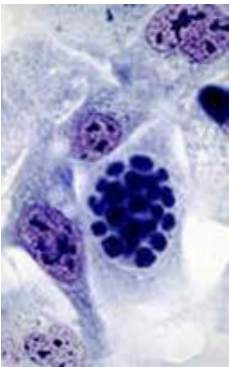
The Peru group continue to be active and in addition to the strong research output in 2007 have hosted both The Wellcome Trust Latin America Meeting and The Imperial College Centre for Clinical Tropical Medicine annual jamboree. I am pleased to say that both these occasions were great successes and in particular, it was good to see the extremely high quality of international presentations from collaborators from around the world particularly those working in the laboratories and field sites in Peru.

I am looking forward to working with everyone over the next 6 months and there is a lot to anticipate including the initial steps towards formation of the first UK Academic Health Sciences Centre – the consultation for this has started, so do contribute. In addition, our excellent seminar series organised by Danny Altmann is about to join more formally with the seminars in the Department of Immunology. This will create the John Humphrey Seminar Series which I have no doubt will be extremely stimulating. Finally and just in time for the change in weather, I am pleased to say that drinking water has been made available to everyone once again!

**Jon Friedland**

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# Teaching & Learning



## Update in Infectious Diseases 2007

The second Update in Infectious Diseases short course took place on 19th and 20th March at the South Kensington Campus.

The two day course held by the Department of Infectious Diseases and Immunity, organised by Charlotte Burt and Jon Friedland, was for the second year running a great success. Demand for places was extremely high with a waiting list of hopefuls. The audience varied from Imperial College medical students, to Surgical MSc students and ID Physicians from around the country. This mirrored the diversity of the speakers which included many guest lecturers from the UK and abroad.

Specific topics relating to the four main course areas were explored by each speaker. Day one focused on **Infection & Immunity**, chaired by Prof. Jon Friedland followed by **Surgical Infections**, chaired by Dr Shiranee Striskandan.

On the second day Dr Alison Holmes chaired the morning session on **Hospital Acquired Infections**, with Dr Dan Agranoff chairing **Emerging Infections** in the afternoon.



Prof Jan Kluytmans

Professor Jan Kluytmans from Amphia Hospital in the Netherlands gave an interesting talk on multi-drug resistant hospital infections, presenting a very different experience from hospitals in the Netherlands where the prevalence of MRSA is still less than 1%!



Dr Nick Maskell

Dr Nick Maskell from Southmead Hospital, Bristol gave an extremely practical lecture on the management of Empyemas which was particularly useful for all the junior doctors in the audience.

Stimulating and engaging lectures were given by invited speakers: Professor Pillay and Professor Singer from UCH, Dr Jerry Brown from UCL and Jennie Wilson from the HPA. There were exciting talks from Imperial colleagues Professor. Van Dellen and Professor. Ferguson OBE and also from members of our department including Dr Striskandan, Dr Newsholme and Dr Bamford



Dr Jerry Brown



Prof Neil Ferguson OBE

Dr Joe Keane, from Trinity College Dublin lectured enthusiastically about the very topical subject of 'TNF and Tuberculosis: from Bench to Bedside'.



Dr Joe Keane



Prof Deenan Pillay

It was an extremely informative 2 days, and discussing with colleagues afterwards there was already great enthusiasm for next years course, hopefully with an improved Peruvian connection!

For the finale there was a live link up for clinical cases with Dr David Moore from Peru but unfortunately the sound failed, so Dr Rod Escombe, recently returned from Lima, stepped in to give a fascinating talk on his research into containing the spread of airborne TB.

See page 4 for more on Dr Rod Escombe's work



Dr Rod Escombe



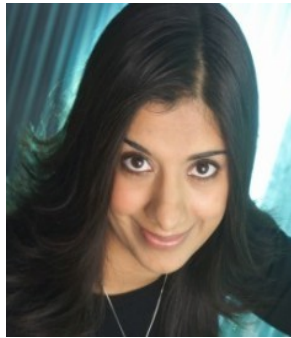
Jennie Wilson

Sophie Yacoub  
Academic Clinical  
Fellow

## Staff's Eye View

**Kavita Mirpuri, PA to the Head of Department, talks about her work as part of the department's administrative team.**

I joined the department at the end of 2001 as the Team Secretary working for various personalities with the department. It did not take me long to learn how to prioritise my work load and to identify a routine that that pleased all!



My daily tasks range from writing e-mails, audio typing, and taking minutes. There's also a range of more one-off tasks to keep me occupied, recently I perfected my badge making skills for delegates attending the Update in ID short course.

Many of my tasks involve interacting with members of the department which I thoroughly enjoy and feel that I have got to know many of the support staff, senior staff and students very well during my time here.

At the end of 2005 I felt that it was time to move on from my current position and was appointed as PA to Jon Friedland, Head of Department. During my time in this post I have really enjoyed working on grant applications and was thrilled when all my hard work on a recent HHTRC grant paid off for the department to get a luminex machine! I look forward to the next application and hope we are as successful!

**Kavita Mirpuri**

## Health & Safety News

Most of the noisy works are almost completed for the 8<sup>th</sup> floor, and as a consequence, there will be less banging from above, missing ceiling tiles and leaks hopefully very soon. Thanks to the stand the Department has taken on some lax practices towards H&S College rules, contractors' attitudes have immensely improved in the past weeks, and the number and range of problems on the floor has fallen.

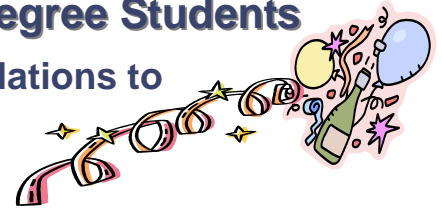
Personal safety is also paramount while on the 7<sup>th</sup> floor. Remember that you are within your rights to ask to see someone's security pass, and if they fail to show their pass, to call Security on 3333.

The refurbished 8<sup>th</sup> floor will feel much more secure, so remember it's only a few months away!

**Frederique Guesdon**

## Research Degree Students

### Congratulations to



**Aceel Al-anizi  
Madeline Stone  
Claire Turner**

**Who recently successfully completed their MPhil to PhD upgrades**

**Debra Harris  
James Harris  
Philip Hopkins  
Cecilia O'Kane  
Tina Miles**

**Who were all recently awarded their PhD**

### Well Done to All!

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#### Staff, Student & Alumni Prizes & Appointments

As well as being awarded his PhD, in October **Dr Philip Hopkins** won the Gold Medal at this year's Intensive Care Society (ICS) meeting

**Dr Alison Holmes** was appointed as an Expert member of the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infections, for a three year tenure from the beginning of June 07

**Dr Dan Agranoff** and **Dr Frances Sanderson** were recently conferred fellowship to the Royal College of Physicians

**Prof Jon Friedland** has been appointed as an expert member to the National Expert Panel on New and Emerging Infections which is advisory to the Chief Medical Officer

**Prof Sunil Shaunak** was named as one of Fortune Magazine's top 24 Innovators ("...innovators, entrepreneurs or just good old fashioned trouble-makers!"). Sunil captured their attention with his work on a cost effective PEGylated-interferon for Hepatitis C in the context of an Imperial College spinout company called PolyTherics.



[http://money.cnn.com/magazines/fortune/fortune\\_archive/2007/05/14/toc.html](http://money.cnn.com/magazines/fortune/fortune_archive/2007/05/14/toc.html)



## In print.....

### Dr Rod Escombe discusses his paper on airborne TB which recently appeared in PLoS Medicine

Tuberculosis (TB) is transmitted by airborne droplet nuclei, produced by the evaporation of larger droplets resulting from respiratory manoeuvres such as coughing, talking, or sneezing. These 1-5µm diameter particles have negligible settling tendency, and remain suspended in the air for long periods. They are sufficiently small to bypass upper airway defences reaching the alveoli of a susceptible host, to establish new infection and thus continue the epidemic of this ancient disease.



Hospital de Dos Mayo

Institutional TB transmission has long been a problem, with numerous outbreaks reported in hospitals, homeless shelters, prisons, and schools. Nosocomial TB transmission is increasingly recognised as a serious problem in low resource settings, and the majority of the extreme drug resistant (XDR)TB reported in Kwazulu Natal last year (Lancet 2006;368:1575) was thought to be nosocomially acquired. Occupational TB in low resource countries is an increasing public health problem, and exacerbates the loss of health care staff from the developing world.

Preventing TB transmission includes environmental control measures to dilute the number of infectious droplet nuclei in the air. Isolation rooms with mechanical ventilation and negative pressure are the standard of care in the developed world, but are very expensive to install and expensive to maintain. Natural ventilation by opening windows offers a low cost alternative. It is recommended by the WHO for low resource settings, but until now there were no studies of the rates, determinants or efficacy of natural ventilation in health care settings.



Old-fashioned TB wards in Lima with high ceilings and big windows.

We measured room ventilation in a variety of settings in 8 different hospitals in Lima, Peru, using a carbon dioxide tracer gas technique.

Rooms studied included TB wards and clinics, respiratory, HIV and infectious diseases wards, respiratory out-patient clinics, waiting rooms and emergency departments.

We compared these with 12 mechanically ventilated isolation rooms. We were surprised to find very high levels of ventilation in the naturally ventilated wards: a median 29 air-changes/hour, compared with the 12 air-changes/hour recommended by guidelines for mechanically ventilated rooms. This advantage was maintained even on days with little wind. Ventilation was greatest in old fashioned wards, many of which were built over 50 years ago specifically for TB patients using the design principles of Victorian TB sanatoria, with high ceilings, balconies and large windows.

There were median 40 air-changes/hour in such rooms. We used a mathematical model of airborne infection to predict much lower risks of TB infection in naturally ventilated wards compared with the 12 air-changes/hour of mechanical ventilation, and protection against infection was greatest in the old-fashioned wards

Natural ventilation is obviously climate dependent, but with the highest burden of TB being in the tropics, opening the windows offers an important control measure in the fight against TB. Owing to its cost, negative

pressure mechanical ventilation must be limited to small high-risk areas. A great advantage of natural ventilation is its applicability to a



wide variety of hospital settings including waiting rooms, out-patients clinics and emergency departments, the very places where undiagnosed, untreated and therefore the most infectious TB patients are likely to be found.

Natural ventilation also has an important role to play in the roll-out of enhanced HIV care, where highly susceptible people are congregated in frequently overcrowded settings with the very people likely to have high rates of TB and drug resistant TB – the perfect recipe for TB transmission.

## Research report

Nicolette Davies reports on the Wellcome Centre 12th Annual Scientific Meeting and Wellcome Trust Latin America Network Meeting held in Peru at the beginning of March 07.

The Wellcome Centre's 12<sup>th</sup> Annual Scientific Meeting was held in Lima, Peru where four of our Fellows (Carlton Evans, David Moore, Rod Escombe and Gurj Sandhu) continue to work in remarkable surroundings. The Wellcome Trust had also decided to hold their Latin America Network Meeting the same week at the same venue; a fantastic opportunity for an integrated infectious disease meeting.

Upon arriving in Lima, the hustle and bustle at the airport gives a small introduction to the chaos that the city offers; characterised by noise, bright colours and taxi drivers with a death wish.

On Monday morning David organised a site tour for Wellcome Trust and Imperial College staff. The tour began at the Health Centre run for the 350,000 population of

Pampas shanty town on the outskirts of Lima. The hour spent in grid locked traffic highlighted the challenges faced by



commuting between sites. Driving through the shanty town which is based on desert, the extent of extreme poverty soon became apparent.

Rod had organised a tour of Hospital de Dos Mayo where we met the Director and clinical staff working on the TB and HIV wards. We visited the research facility built on the roof of the TB ward, where



Rod's ventilation project was successfully implemented and for which he is now a local celebrity, having his picture published in local newspapers. The tour included the mausoleum of Daniel Carrión, the Peruvian medical student after whom Carrion's disease was named.

The Universidad Peruana Cayetano Heredia was the final destination of the site tour, an opportunity for Bob Gilman, and our Peruvian collaborators to present their research. As we toured the laboratories the scope of research became apparent, with projects ranging from investigating immune responses to neurocystercycosis to diagnosis of TB using images from a mobile camera phone.



The Wellcome Trust commenced their Latin America Network Meeting with the Populations and Public Health items. This was followed by The Infectious Disease section and included sessions on Parasitic Infections, TB, STIs and HIV/AIDS. Carlton presented his Innovative Strategies for TB Control project. David and Rod presented 'Getting Research into Policy and Practice' case studies: with David speaking on MODS for diagnosis of MDRTB, and Rod discussing research on natural ventilation for the prevention of nosocomial TB transmission.

The Wellcome Centre's meeting began with Jimmy Whitworth (Head of International Activities at the Trust) presenting an overview of Wellcome funded Fellowships. Three sessions were held on Thursday exploring TB Control, Diagnosis and Treatment. Imperial College was widely represented with David, Carlton, Rod, Gurj and Dan Agranoff presenting. A large group of students from Peru, Imperial College and the USA also presented fascinating research including 'stool testing to diagnose pulmonary TB in adults and children', 'TB skin test, nutrition and disease status' and 'weight change to predict TB treatment outcome'.

In the evening The Royal Society of Tropical Medicine and Hygiene Centenary held a celebration special lecture and reception with Geoff Pasvol presenting an introduction to the Society, followed by an entertaining and informative lecture on 'Cysticercosis: understanding an infection' given by Hugo Garcia and Emico Gonzalez.

The final day was split into three sessions: TB Immunology and Pathogenesis, TB and more and Tropical Medicine in the Tropics, providing a diverse and interesting range of talks. On both days there was an excellent series of talks attended by 120 people from various research groups.

Most importantly this international meeting provided an opportunity for researchers in the field to present and discuss the scope of TB research taking place in Peru.



# Calendar of Events

## Research Seminars

Research in Progress meetings take place each Thursday lunchtime.  
Recent and future speakers:

24th May Prof Uta Griesenbach  
Imperial College London  
**'Progress in CF Gene Therapy'**

14th June Dr Neil Young  
University of Cambridge  
**" The Leucocyte Receptor Complex - Novel Functions in Immune Regulation"**

31st May Prof Anne Cooke  
University of Cambridge  
**Infection and Autoimmunity: are we winning the war only to lose the peace?**

21st June Prof Oresto Acuto  
University of Oxford  
**"Tailoring TCR signals by feed-back mechanisms"**

7th June Prof Graham Rook  
University College Medical School  
**'Immunotherapeutics that are active without chemotherapy in murine pulmonary tuberculosis; is there a common pathway and can we exploit it for XDR-TB?'**

12th July Dr Ben Wakerley  
Imperial College London  
**"Replicative history of T cells in Multiple Sclerosis"**

28th June Prof Martin Goodier  
Imperial College London  
**'Factors influencing Natural Killer cells in HIV-1 infected individuals and the effects of anti-retroviral therapy'**

## Clinical Academic Seminars

The Department hosts a regular **Clinical Academic Seminar** series.  
Recent & future guest speakers include:

10th April Dr Chris Conlon  
John Radcliffe Hospital, Oxford

12th June Dr Pam Das  
The Lancet Infectious Diseases

8th May Prof. Anthony Costello  
Institute of Child Health

3rd July Dr Vas Novelli  
Gt. Ormond Street Hospital for Children

## In the press

Professor Sunil Shaunak received wide-spread media coverage for his work with Prof. Steve Brocchini (London School of Pharmacy) to develop and manufacture a cost effective PEGylated-interferon for Hepatitis C. The project is supported by the Wellcome Trust and BBSRC with clinical trials scheduled to take place in India next year. Coverage included The Guardian (front page) and Channel Four News

### The Guardian 02/01/07

Scientists on a mission to bring cheap drugs to the world's poorest countries  
<http://education.guardian.co.uk/higher/news/story/0,,1981356,00.html>

### The Guardian 02/01/07—Scientists Find Way to Slash Cost of Drugs

The  
<http://education.guardian.co.uk/higher/news/story/0,,1981354,00.html>

Health Protection Matters: Issue 7 included Liz Hall's article "A Pharmacy First" in which she discusses the development of the MSC in Infection Management for Pharmacists and the triangular collaboration between academics, healthcare professionals and practitioners.

### Hammersmith Research

Issue 40, spring 2007  
"Team Tackles a Deadly Toxin" highlights the project led by Dr Shiranee Sriskandan to shed more light on PVL and its effects on patients.



### Selected recent publications from the Department of Infectious Diseases & Immunity

Anderson, A.E., Worku, M.L., Khamri, W., **Bamford, K.B.**, Walker, M.M., Thursz, M.R. *TLR9* polymorphisms determine murine lymphocyte responses to *Helicobacter*: Results from a genome-wide scan. *Eur. J. Immunol.* 2007; **37**: DOI:10.1002/eji.200636562.

Cartwright, N., McMaster, S.K., Sorrentino, R., Paul-Clark, M., **Sriskandan, S.**, Ryffel, B., Quesniaux, F.J., Evans, T.W., Mitchell, J.A. Elucidation of toll-like receptor and adapter protein signaling in vascular dysfunction induced by gram-positive *Staphylococcus aureus* or gram-negative *Escherichia coli*. *Shock.* 2007; **27**: 40-47.

Edwards, R.J., Wrigley, A., Bai, Z., Bateman, M., **Russell, H.**, Murray, S., Lu, H., Taylor, G.W., Boobis, A.R., **Sriskandan, S.** C-terminal antibodies (CTAbs): A simple and broadly applicable approach for the rapid generation of protein-specific antibodies with predefined specificity. *Proteomics.* 2007; **7**: doi:10.1002/pmic.200600916.

**Escombe, A.R.**, Oeser, C.C., Gilman, R.H., Navincopa, M., Ticona, E., Pan, W., Martinez, C., Chacaltana, J., Rodriguez, R., **Moore, D.A.J.**, **Friedland, J.S.**, **Evans, C.A.** Natural ventilation for the prevention of airborne contagion. *PLOS Medicine.* 2007; **4**: doi:10.1371.

**Harris, J.E.**, **Fernandez-Vilaseca, M.**, **Elkington, P.T.G.**, Horncastle, D.E., Graeber, M.B., **Friedland, J.S.** IFN $\gamma$  synergizes with IL-1 $\beta$  to up-regulate MMP-9 secretion in a cellular model of central nervous system tuberculosis. *The FASEB Journal.* 2007; **21**: 356-365.

Zloh, M., **Shaunak, S.**, Balan, S., Brocchini, S. Identification and insertion of 3-carbon bridges in protein disulfide bonds: a computational approach. *Nature Protocols.* 2007; **2**: 1070-1083.

Isaacs J.D., **Ingram R.E.**, Collinge J., **Altmann D.M.**, Jackson G.S., The Human Prion Residue 129 Polymorphism Lies Within a Cluster of Epitopes for T Cell Recognition. *J Neuropathol Exp Neurol.* Vol 65, number 11, Nov 2006

**Moore, D.A.J.**, Caviedes, L., Gilman, R. H., Coronel, J., Arenas F., LaChira, D., Salazar, C., Saravia, J. C., Oberhelman, R. A., Hollm-Delgado, M-G., **Escombe, A. R.**, **Evans, C. A. W.**, **Friedland, J.S.** Infrequent MODS TB culture cross-contamination in a high-burden resource-poor setting. *Diagnostic Microbiology and Infectious Disease* 56 (2006)35-43

**Harris, J.E.**, **Green, J.A.**, **Elkington, P.T.**, **Friedland, J.S.** Monocytes infected with *Mycobacterium tuberculosis* regulate MAP kinase-dependent astrocyte MMP-9 secretion. *Journal of Leukocyte Biology.* 2007; **81**: 548-556.

**Harris, J.E.**, Nuttal, R.K., **Elkington, P.T.**, **Green, J.A.**, Horncastle, D.E., Graeber, M.B., Edwards, D.R., **Friedland, J.S.** Monocyte-astrocyte networks regulate matrix metalloproteinase gene expression and secretion in central nervous system tuberculosis in vitro and in vivo. *The Journal of Immunology.* 2007; **178**: 1199-1207.

**O’Kane, C.M.**, Boyle, J.J., Horncastle, D.E., **Elkington, P.T.**, **Friedland, J.S.** Monocyte-dependent fibroblast CXCL8 secretion occurs in tuberculosis and limits survival of mycobacteria within macrophages. *The Journal of Immunology.* 2007; **178**: 3767-3776.

Reynolds, C., Ozerovitch, L., Wilson, R., **Altmann, D.**, Boyton, R. Toll-like receptors 2 and 4 and innate immunity in neutrophilic bronchiectasis. *Thorax.* 2007; **62**: 279.

**Sriskandan, S.**, **Faulkner, L.**, **Hopkins, P.** *Streptococcus pyogenes*: Insight into the function of the streptococcal superantigens. *The International Journal of Biochemistry & Cell Biology.* 2007; **39**: 12-19.

von Delwig, A., **Altmann, D.M.**, Charlton, F.G., McKie, N., Isaacs, J.D., Holmdahl, R., Robinson, J.H. T cell responses to a non-glycosylated epitope predominate in type II collagen-immunised HLA-DR $\beta$ 1\*0101 transgenic mice. *Ann Rheum Dis.* 2007; **66**: 599-604.

Thomas, L.H., Wickremasinghe, M.I.Y., **Friedland, J.S.** IL-1 $\beta$  stimulates divergent upper and lower airway epithelial cell CCL5 secretion. *Clinical Immunology.* 2007; **122**: 229-238.

**Escombe, A.R.**, Oeser, C., Gilman, R.H., Navincopa, M., Ticona, E., Martinez, C., Caviedes, L., Sheen, P., Gonzalez, A., Noakes, C., **Moore, D.A.J.**, **Friedland, J.S.**, **Evans, C.A.** The detection of airborne transmission of tuberculosis from HIV-infected patients, using an in vivo air sampling model. *Clinical Infectious Diseases.* 2007;44:1349-1357

Mitchel, P., Germain, C., Fiori, P.L., Khamri, W., Foster, G.R., Ghosh, S., Lechler, R.I., **Bamford, K.B.**, Lombardi, G. Chronic exposure to *Helicobacter pylori* impairs dendritic cell function and inhibits Th1 development 2007; **75**: 810-819

## Out & About: Christmas Party 2006

With summer quickly approaching, memories of winter, and the 2006 fog, have faded. However, we find sometime to reflect on the past year and the 'best Christmas party ever.'

The Infectious Diseases Department kicked off the 2006 holiday season with its annual staff Christmas party. It was held in Hammersmith at the Dartmouth Castle and was, by and large, a success. With the combination of nibbles (most of which ended up on the floor), wine and good company the only complaint was the unsurprising lack of food and some slightly suspect black pudding. Both of which were blamed for various departmental illnesses the next day and a, very nearly, missed flight to America.



The night was well attended and provided a time for members of the department to be together as a group. It is hoped that the implementation of the new 'open plan' ID department will operate as smoothly as the holiday party. Although, perhaps without as much food on the floor.



As the night drew to an end the wine and conversation were flowing. A lot has happened since Christmas time and the next seven months promise to be no different.



Notably, there were some early leavers, claiming to 'still be recovering' from the TB lab group Christmas party earlier in the week. It was rumored Justin Green, Dr and star striker for the ID Academicals, had sustained a dancing related injury. (He has assured us he has fully recovered and will be ready for next season.)



One can only hope that next year's Christmas party finds the department happy, healthy, with a little more food and a little less fog.



Liz Hall  
Social Events Correspondent