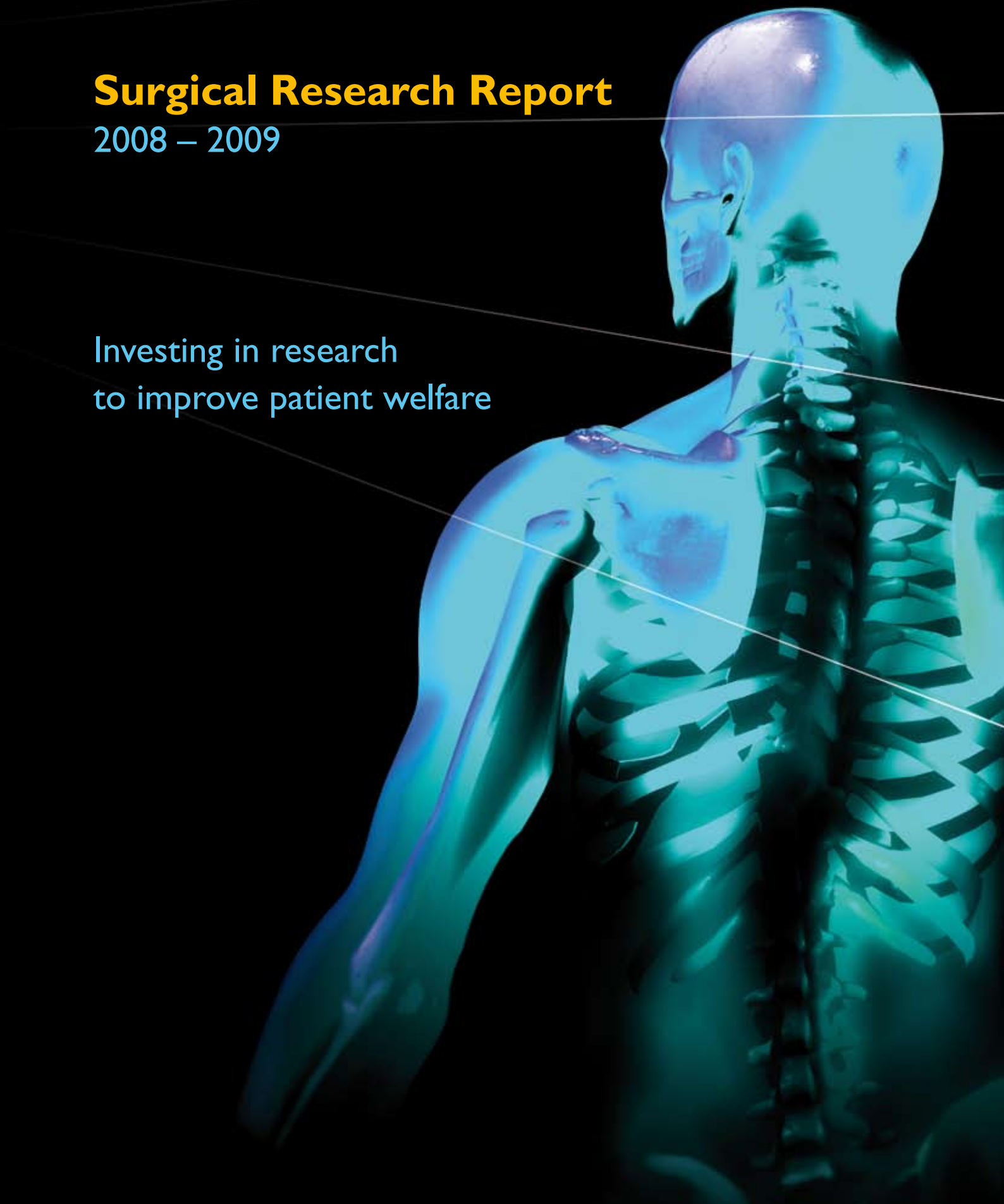
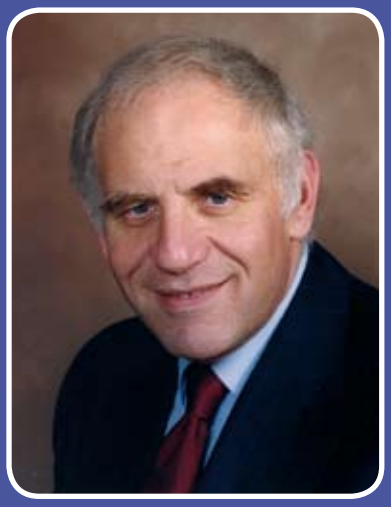
The Royal College of Surgeons of England

Surgical Research Report
2008 – 2009

Investing in research
to improve patient welfare





Professor Norman Williams
Director of the Research Department

introduction
to Research Report 2008-09

Despite the tumultuous changes that are going on in surgical training, research at the College goes from strength to strength. The research fellowship scheme, which has been the jewel in our crown, continues to develop and we are enormously grateful to all those companies, institutions and individuals who have given so generously to the cause.

Our most recent research fellowship awards day is emblematic of the College recognising excellence in research. Initially there were 63 applications for funds and 40 applicants were shortlisted and invited to produce a poster of their forthcoming research – they would then come to the college and be viva'd individually by 8 academic surgeons from across the specialties. 21 awards were made that afternoon amounting to more than £1 million. The standard was of the highest quality. All assessors remarked that had there been sufficient funds they would have wished to have made far more awards. All of this highlights our continued need for more funds: Martyn Coomer and his team are continually exploring new sponsors and ways of increasing the research fellowship portfolio, for which we are particularly grateful.

Resourcing surgical research could be considerably aided if the surgical community were less reticent at blowing its own trumpet concerning its achievements in improving health care via research. Although reticence is not normally an adjective that readily springs to mind when describing surgeons, there is no doubt that surgical research in recent years has taken a back seat when compared to basic science. However, without the translational skills that surgeons possess there is little doubt that many of the basic science breakthroughs of today will not be deliverable into the clinic and ward tomorrow. One only has to look back to see how these translational skills have revolutionised health care.

Transplantation would never have developed without the clinical and scientific input of the early surgical pioneers and it is no coincidence that one of them, James Murray, received a Nobel Prize for his endeavours. Similarly, the whole field of joint replacement could not have developed without the application of physics and material science by John Charnley. Modern cardiac surgery was primarily a fusion of surgical, physiological and engineering endeavours as indeed is minimally invasive surgery. There are many other examples but in recent years these achievements have received scant regard and the lack of investment within our universities and medical

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Compiled by Linda Slater. Designed and produced by Avid Creative Ltd. Printed by Riverprint Ltd. Edited by Jon Hackett.
Photography by John Carr and Martyn Coomer.

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schools has resulted in a downgrading of applied clinical research, particularly in the craft specialties. That the folly of this has finally been realised, is some compensation but it will take some years to rebuild the infrastructure that has been damaged.

Nevertheless, with the introduction of the Walport initiative and 'new blood' senior lectureship scheme a new career structure has been introduced for the budding clinical academic. This College has been particularly active in ensuring that surgery is well represented in the award of these posts and I am pleased to report that we are now second in the league table of posts awarded. All surgeons, no matter their background and interests, should applaud and support these developments as thriving academic departments of surgery can only benefit the profession as a whole, encouraging and nurturing the surgical scientists of the future who will take our profession to new heights.

These developments and others such as Best Research for Best Health underline the rapidly changing landscape and it is essential that this College remain in the forefront of clinical research. With this in mind the research board is conducting a review of its activities to determine how best the College resources can be utilised in the coming decade for the benefit of fellows and members. The first part of this was a scoping exercise carried out at Southwark Cathedral. This was an extremely successful exercise, which highlighted the need for a pan-college approach. There were also calls for basic research training for all trainees, research opportunities for all trainees together with a research component to be built into a-post CCT clinical fellowship scheme. (see page 8)

Part of the research board's portfolio is to oversee the Clinical Effectiveness Unit and the National Collaborating Centre for Acute Care (NCC-AC), both of which are becoming very important in the changing health care environment. It is imperative for the College to have at its fingertips high-quality data especially when it comes to surgical performance. The CEU under the direction of Dr Jan van der Meulen has the expertise to do this. It has an important collaboration with the London School of Hygiene and Tropical Medicine, one of the world's foremost epidemiological research institutions.

Consequently, studies emanating from the unit are high calibre and well respected. It is no coincidence that Jan and colleagues have just been awarded a contract to investigate the outcome for patients treated in ISTCs. Their input into how best to collect data for revalidation will in future years will be of considerable importance to all fellows and members. Similarly, the NCC-AC, under the direction of Dr Jennifer Hill, will have increasing influence on the work surgeons do by determining for the National Institute for Health and Clinical Excellence which management pathways should be followed and which should be abandoned.

As part of the review mentioned above we will look at the composition of our research board membership to ensure it is representative of the entirety of surgical specialties. However I should like to state on the record that such a review has nothing to do with the calibre, enthusiasm and commitment of present members who do a brilliant job in assisting Martyn and I in the assessment of the fellowship applications and in developing strategy. Another acknowledgement I should like to make is to my predecessor Tony Mundy who steered the ship with considerable aplomb and foresight over the five years preceding my appointment in September 2006. There is no doubt that his stewardship has left the College's research capabilities in a very strong position. He will be a hard act to follow.

in pictures

UK

1 President talking to a patient at Trafford ISTC.

2 President opening educational/ information unit at Stepping Hill Hospital, Stockport.

3 Mayoni Goonerate undertaking the raffle at Somerset WI Western Super Mare research evening.

4 Sir Leszek Borysiewicz (new chairman MRC) addressing Council.

5 President with Mr Per Sandquist at Shepton Mallet Treatment Centre.

6 Mr Richard Regan, Chairman of the Oversight Committee, with the President.

7 Professor Janet Wilson making a point at the special meeting on Academic Clinical Fellowships.

8 Jayne Taylor and James Duffy on the RCS Career Development Programme meeting Lord Darzi at St Mary's Hospital Paddington.

9 Professor Sir Peter Bell, Professor Sir Peter Morris and Professor Maurice Lessof at the Joint Dunhill Medical Trust Research Fellowship interviews.

10 Staff watching operation at St Mary's Hospital.

11 President addressing trainees and consultants about the MTAS fiasco at Wythenshaw Hospital, Manchester.

12 Professor Norman Williams with Dr Elizabeth Rang and Mr John Hartley at the ia research fellowship interviews outside the Royal London Hospital research laboratories.

13 Dr Mike Stroud with Susan Murray and Louise Thomas from NCC-AC working on the nutrition guidelines.

14 Miss Anne Moore, Vice President, visiting skills centre in Torbay.

united kingdom


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UK continued

15 Loyal supporters Mr Trevor and Mrs Lyn Shears, and Mr Hywel Jones of the Development Office, outside SAGE in Newcastle.

16 Lord Wolfson opening phase 1 of the Eagle Project.

17 President opening HPB Masterclass with Mr Russell.

18 Mr Richard Shaw addressing the Grand Lodge 250th anniversary Committee.

19 Preparing to meet the Minister of Health and CMO for Northern Ireland at Westminster.

20 Dr Richard Taylor independent MP from Kidderminster.

Hereford 6th Form College

21 Miss Bynvant Sandhu teaching suturing.

22 Mr John Black explaining basic laparoscopic skills.

23 Miss Elly Breuning teaching knot tying.

Research Strategy Day, Southwark Cathedral

24 Sir David Cooksey presenting his report.

25 Professor Arnie Hill presenting an Irish viewpoint.

Welsh Board

26 Mr Wyn Lewis delivering Hunterian Lecture at Welsh Surgical Society.

27 President explaining to trainees about MTAS at the Welsh Surgical Society.

28 Welshboard enjoying a drink after the meeting in Caerleon.

29 Mr Brian Gibbons former Minister of Health, Welsh Assembly Govt.

in pictures

Ghana Trip

30 Basic Surgical Skills workshop faculty and participants in Accra.

31 Mr Steve Mannion demonstrating thoracic trauma in a workshop.

32 Jan Van der Meulen teaching statistics at Korle Bu Hospital, Accra.

33 Jim Armitage capturing the audience at Korle Bu Hospital, Accra.

34 Paul Cathcart teaching research methods at Korle Bu Hospital, Accra.

35 President being awarded an honorary fellowship from The Ghana College of Physicians and Surgeons.

Ethiopia Trip

36 Celebrating the 80th birthday of Professor Eldryd Parry in Gondar.

37 Wheelchair bound physiotherapist practising at the Fistula hospital Addis Ababa.

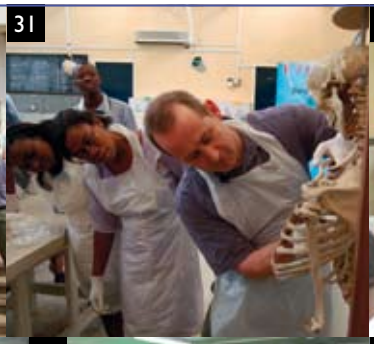
38 Mrs Elizabeth Ribeiro teaching physiotherapy at the Fistula hospital.

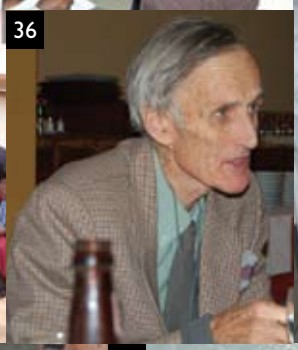
39 President examining thyroid patient in Gondar Hospital.

40 Mr Gordon Williams, Mrs Elizabeth Ribeiro, Dr Catherine Hamlin and the President at the Fistula hospital.

41 Shotgun wound on ward round at Gondar Hospital.

42 Presenting textbook of tropical surgery to Dr Birhanu Kotiso, Professor of Surgery, Black Lion Hospital, Addis Ababa.





africa, asia, caribbean

Ethiopia Trip continued

43/ Patients from the Fistula hospital
44 learning domestic and farming skills before returning home.

Malawi Trip

45 Mrs Ribeiro at the Open House orphanage Blantyre, Malawi.

46 President with Mr Nyengo Mkandawire, President of COSECSA in Malawi.

Jamaica Trip

47 Mr David Rosin teaching at laparoscopic workshop in Kingston, Jamaica.

48 Professor Mike Bailey improvising with a cardboard box at a laparoscopic workshop in Kingston, Jamaica.

49 The Basic Skills Faculty in Kingston, Jamaica.

Voyage of the Eagle, RCS triennial trip to China and Hong Kong

50 A trio of Presidents in Hong Kong Harbour.

51 Presenting to the Freemasons of Hong Kong.

52 Watching an operation in 3D in The Chinese Unversity of Hong Kong.

53 President with Mr Colin Morgan of Ethicon outside the new J&J skills centre Beijing.

54 Professor Zhang Jin-Zhe, founding father of paediatric surgery in China, receiving an Honorary Fellowship in Beijing.

the College's role in research
– a vision for the future

Research is the lifeblood of any professional group. Without the exploration of new ideas a discipline has no hope of developing and moving forward. Surgery is no exception and this College is committed to pursuing its research portfolio and providing opportunities to all its fellows and members. It should be understood that the president and Council are absolutely committed to ensuring that research is very much a part of the education of all who wish to pursue a career in surgery.

That is not to say that research should be used as the only discriminatory criterion for entering training, a failing which has been a particular criticism of the old selection process. On the other hand, to ignore the academic prowess of applicants would be a mistake and it is encouraging to see that the review of MMC by Sir John Tooke and colleagues recognise research activity in a more positive light. There can be no doubt, however, that the emphasis of the College must be in providing opportunity to those individuals who have been selected for training. We, as custodian of College funds, have a responsibility for ensuring that research monies are targeted at appropriate problems, investigated to the highest standard and carried out by committed individuals who wish to genuinely move their specialty forward.

We also have a duty to ensure that all fellows and members have an appreciation of what research is about so they can be discriminatory in the papers they read and be able to sort fact from fiction. We have a responsibility to support the academic departments of surgery, which provide the environment for research to be undertaken and which in recent years have been decimated by a flawed medical research policy. That this policy has at last been recognised to have failed particularly in the fields of applied clinical and translational research is some compensation but it will take time and effort to restore what in many people's eyes was a jewel in the crown of the UK health care system.

Nevertheless, we have been heartened by the Walport initiative whereby perhaps for the first time a clinical academic career pathway has been established and supported by central funding.[1] Initially surgery did not do well in the competition for these posts, but with appropriate pressure from this College the number of posts dedicated to the surgical disciplines has increased to become second in the league table. This indeed is an encouraging start but more needs to be done, much of which is in our own hands.

Sir David Cooksey and Professor Norman Williams, Chairman, at the Research Strategy Day, Southwark Cathedral.

With these thoughts in mind the research department at the College decided to initiate a review of its research activities. This is ongoing and the following is still very much an interim report of current thinking – but we hope it points a way for the future. In order to advance thinking a 'scoping exercise' at Southwark Cathedral was convened in April of this year. All interested parties, including trainee representatives, were invited. We also invited various speakers with particular expertise to give presentations from their perspective as to where surgical research should be going. In particular we had the pleasure of welcoming Sir David Cooksey, the chairman of the Government's review group on medical research, which had come out so strongly in favour of translational research.[2]

Interestingly, Sir David was extremely positive towards research being carried out by surgeons. The turnout was impressive and the discussion lively . There was strong support for the College signalling its commitment to research by providing a variety of appropriate opportunities along the surgical career path – from the initial stages of training through to the early consultant years. The argument was for flexibility, and supporting a variety of routes into research, rather than focusing solely on the Walport route. It was agreed that:

- All trainees will be expected to have a basic knowledge of i) research methodology, ii) statistical methods, and iii) how to assess and critique a publication. For the College the issue is how best to deliver this training and how to work collaboratively with SACs and deaneries to this end. Delivery may well be implemented via a modular course.
- The College should continue to support non-academic (non-Walport) trainees with a serious interest in research. There are issues to be resolved around routes into such awards (application criteria) and routes out (opportunities for progression); also around the timing of such awards (early or late in training).

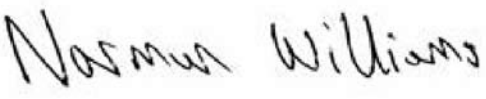
- There is a case for using College funding to support the Walport initiative – specifically to provide clinical scientist posts to bridge the gap between academic fellowships and lectureships; it was suggested that such posts might be joint-funded by the College and the UKCRC.
- There might also be a case for providing a limited number of pump-priming grants for young consultants, but this kind of work (which is mainly translation) should by and large be funded by the Cooksey arrangements
- There is a role for clinical fellowships at the end of CCT, in order to offset the effects of shorter training periods under Calman/MMC; such fellowships should include a research element either in clinical research or in areas such as education, policy, management and health economics.
- SACs should have an academic subcommittee to promote the research agenda.
- Faculty development is critical – given the need for inspiring role models and mentors; and those assessing trainees on the curriculum need to have the appropriate knowledge and skill themselves.

It was also recognised that the College needs to promote a multidisciplinary research agenda and that its own research endeavours need to be more coordinated. Thus there is a place for crossing the boundaries of biomedical and educational research. Such an approach is well illustrated by total mesorectal excision for rectal cancer which initially relied on pathological and physiological data to show the technique was feasible and might be beneficial.3 Heald then went out to educate surgeons, particularly in Scandinavia, and demonstrated how such educational programmes could improve survival and recurrence within a population.

The new Wolfson surgical skills centre, phase one of the Eagle Project.

The College also needs to be more proactive in identifying key areas in which surgical practice is expected to develop over the next decade – and which therefore are likely to be priority areas for research. The College's leadership role also implies that it needs to be more proactive in fostering the wider national network of surgical trainees and consultants engaged in research of various kinds. The College has the potential to provide a national forum for discussion and networking – and also to offer a wide range of resources and support including courses, e-learning, conferences and publications.

This is clearly an ambitious programme and not all aims will be deliverable or in fact realistic in the short term. Much effort is required to hammer out a policy that all can sign up to. Council has yet to debate these issues but it is hoped that within the next few months a firm policy will evolve and then an action plan initiated. At this stage we would welcome any ideas or comments from any member or fellow – so please feel free to send your comments to research@rcseng.ac.uk. A final thought: research by its very nature defines the future travel of a profession, it cannot stand still – the College research policy must be dynamic and forward looking: the status quo is not an option.



Norman S Williams
August 2007

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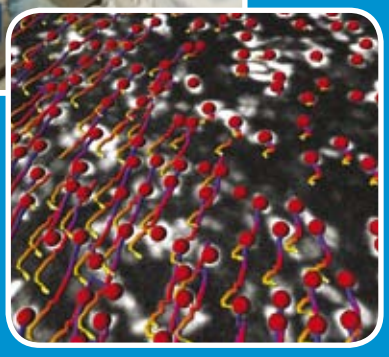
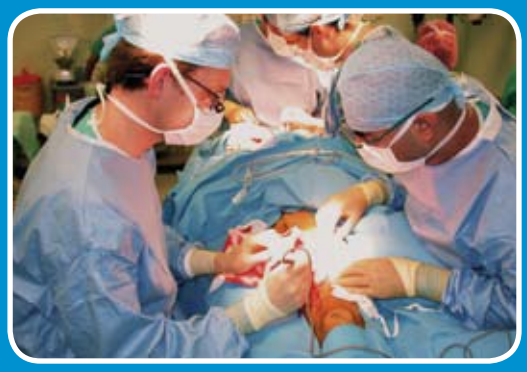
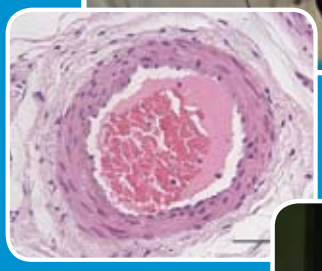
1 Report of the Academic Careers Subcommittee of Modernising Medical Careers and the UK Clinical Research Collaboration, March 2005.

2 Sir David Cooksey. *A review of UK health research funding*. London: HMSO; December 2006.

3 Heald RJ Husband EM Ryall RJ. The mesorectum in rectal cancer surgery – the clue to pelvic recurrence. *Br J Surg* 1982; **69**: 613–16.







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inhibiting
the growth of urinary stones

Physico-chemical factors influencing crystallisation of calcium oxalate in the urinary tract

Millions of people across the world suffer with urinary stones each year. It is one of the most painful afflictions known to man and may have life-threatening consequences. After their first stone, a sufferer left untreated is at a 70% risk of developing another within 10 years. This research project focuses on chemical reactions occurring in urine and the formation of calcium oxalate crystals. It is these crystals that aggregate together to make up the commonest constituent of kidney stones.

Currently, treatment options are limited, including lifestyle changes (such as increasing oral fluids and diet changes), lithotripsy (shockwave therapy used to break stones into smaller fragments) and operations to remove stones. In order to advance treatment, it is necessary to understand the basic interaction between ionic calcium and oxalate and the processes and drugs that may influence crystal formation. Currently very little work is being done in this area.

This research project involved perfecting a model of calcium oxalate crystal formation that closely mimicked the processes in the human kidney. As the chemical constituents of human urine vary widely depending on diet, fluid intake, temperature, etc, it does not provide a stable medium with which to carry out accurate experiments. Therefore we used a well-recognised formula to make up an artificial urine solution. This is highly comparable to the fluid produced within the nephron of the kidney, where crystals first begin to form.

The size of the crystals and the conditions in which they aggregate were then analysed using light diffraction. As the growth of a stone is most influenced by aggregation of crystals rather than individual crystal growth, it was this process that we aimed to interfere with. We tested a range of compounds, with the aim of inhibiting crystal aggregation to prevent them forming the larger particles responsible for so many clinical problems.

The project proved very successful, identifying a group of compounds called bisphosphonates, that have a profound effect on crystal aggregation. These drugs are currently used to treat bone disease with minimal side effects and hold enormous potential for the treatment of stone disease.

'Urinary stone disease affects 12% of the world population, with problems ranging from excruciating loin pain, urinary infections and obstruction of the urinary flow to kidney failure.'

Mixing artificial urine solutions in the laboratory.

Siân with the particle-sizer.

Fellowship/Sponsor
The Newman Foundation RCS Research Fellowship

Miss Siân Allen

Site of study
Institute of Urology & Nephrology, University College London

Further funding
Equipment grant from St Peter's Trust

Supervisors
Mr Simon Choong FRCS Urol
Dr William Robertson DSc
Professor Chris Fry

Presentations

BAUS Section of Endourology, Newcastle-upon-Tyne, May 2006

World Congress of Endourology, Cleveland, August 2006

Société d'Urologie Internationale, Cape Town, November 2006

Prizes

Royal Society of Medicine, Geoffrey Chisholm Prize, May 2006

investigating
the differences in collagen protein production

Fellowship/Sponsor
Dunhill Fellowship

Mr Vipin Asopa

Site of study
Kennedy Institute, Charing Cross Hospital, Imperial College, London

Supervisors
Professor J Saklatvala
Mr R Coombs

Presentations
6th Combined meeting of Orthopaedic Research Societies, Hawaii, October 2007

'Young cartilage produces more collagen than adult cartilage.'

Vipin with a patient.

An investigation into differences in type II collagen synthesis between adult and young articular cartilage

Aims/objectives
To investigate why adults develop osteoarthritis and the young do not.

Methods
Study of adult and young cartilage using western blotting, polymerase chain reaction, and EMSA on animal models.

Results/preliminary findings
Adults produce more collagen protein than the young. There is a 20-fold difference in mRNA levels which can account for this. Sox9 protein levels are 3-fold different between adult and young cartilage and this may account for the differences. Other proteins in the cell could also influence the difference.

Does the research build up on other investigations?
Sox9 directly regulates type II collagen production. It is interesting to show that its levels differ between the adults and the young.

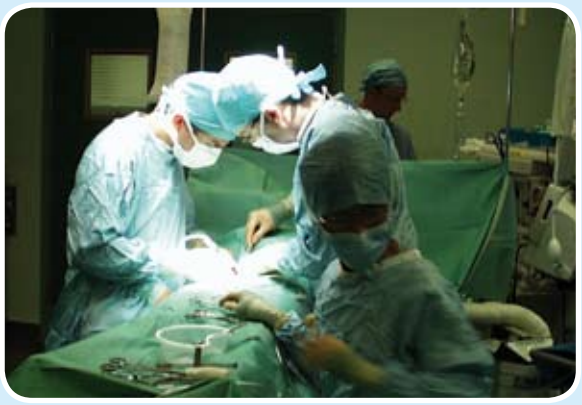
How much research has there been into this area?
There has been very little research looking at the differences between adult and young cartilage.

Is it a long-term project that others will continue to develop?
This project lays the foundations for others to begin to investigate why there are difference in collagen protein production. I have shown that this could be due to differences in Sox9 levels. Understanding this may enable the development of new treatments for osteoarthritis.

What is life like for patients with this condition?
Most people in late life suffer from osteoarthritis. It can affect most joints within the body and causes severe pain and disability and can stop people from carrying out activities of daily living.

How will it improve their quality of life?
Being able to prevent or cure osteoarthritis will change the lives of people all over the world.

determining
the effect of surgery on gene expression



Gary assisting a junior colleague during an appendicectomy.

Fellowship/Sponsor
Freemasons' 250th Anniversary Fund, 2002/2003

Mr Gary Atkin

Site of study
Gray Cancer Institute, Mount Vernon Hospital

Supervisors
Professor George Wilson
Mr John Northover

Publications

British Journal of Cancer 2006; **94**(1): 121–7

British Journal of Cancer 2006; **95**(7): 928–933

Presentations

Society of Academic and Research Surgery (SARS), Newcastle, January 2005

Tripartite Colorectal Meeting, Dublin, July 2005

The effect of colorectal cancer surgery on intratumoural gene expression

Aims / objectives

To determine the effect of surgery on gene expression within cancer cells, looking in particular at those genes that have been used to predict tumour prognosis and the likelihood of a patient responding to chemotherapy.

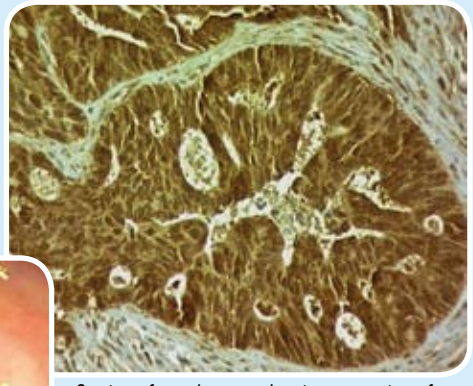
Methods

Samples of rectal cancer were obtained before and after surgery, and the expression of a number of proteins within the rectal cancer cells was measured at both time points. An overall difference in level was calculated for each protein studied.

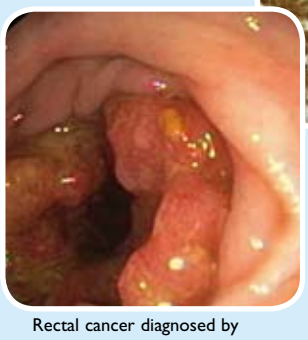
'Bowel cancer is the third commonest form of cancer, with over 33,000 new cases in the United Kingdom every year.'

Results

The level of several proteins was significantly different after surgery, suggesting the environmental stresses encountered during the surgical removal of the tumour (principally a lack of blood supply) are sufficient to alter gene expression levels. These findings highlight the importance of rapidly preserving a tumour's architecture once it is removed from the body, so that any measurement of the tumour's activity performed after surgery is accurate and can be used to guide treatment, such as the need for chemotherapy.



Section of rectal cancer showing expression of one of the studied proteins, thymidylate synthase.



Rectal cancer diagnosed by colonoscopy.

investigating the link
between inflammation and colorectal cancer

Fellowship/Sponsor
University of London

Mr Charles Bailey

Site of study
Imperial College, London

Supervisors
Lord Darzi
Dr David Peck PhD
Dr Rupert Negus PhD

Publications
Clinical and Experimental Metastasis 2007; **24**: 121–130

Presentations
Association of Surgeons of Great Britain and Ireland, Annual Meeting 2003, Manchester, 2003

British Society of Gastroenterology, Annual Meeting 2003, Birmingham, 2003

Charles at work.

The leukocyte and chemokine infiltrate in colorectal cancer and their alteration by preoperative radiotherapy

The purpose of this project was to investigate the link between inflammation and colorectal cancer. Small molecules called chemokines induce the migration of inflammatory cells (macrophages) into areas of inflammation and there is evidence that chemokines are involved in the persistence of inflammation and in the transition from chronic inflammation to cancer. The hypothesis of this project was that chemokines promote the migration of macrophages into human colorectal cancers and thereby influence tumour progression.

This was a science project and experiments were performed on colorectal cancer cells and on solid tumour samples taken immediately after surgical excision. The study found that macrophages increased in number as the cancers became more advanced and that this was due to the tumours producing a specific chemokine called CCL2 (MCP-1). The macrophages were highest is areas with a poor blood supply, areas that are often resistant to radiotherapy and chemotherapy and hence could be used to target treatment to these regions in the future.

In summary the project showed that there is a chemokine network in colorectal cancer that can promote progression by recruiting inflammatory cells and initiating local spread.

'Bowel cancer is the second commonest cause of cancer-related death in the United Kingdom.'

research to reduce
restrictive surgical adhesion formation

The biological treatment of surgical adhesions

'Adhesions may be one of the most common and costly problems in surgery. Occurring after 90% of abdominal operations, they are also common following gynaecological, urological and reconstructive tendon surgery.'

Our aim was to investigate how patient outcomes could be improved by reducing restrictive surgical adhesion formation using novel approaches and treatments.

Our research encompassed several integral areas. We have investigated how the cells of injured tissues contribute to adhesions and how their pathological activity may be blocked. We have developed ways of accurately describing adhesions in terms of their mechanical properties using real-time dynamic 3D assessments. These imaging techniques have enabled adhesions under stress to be directly visualised for the first time, providing new information on why they are such a difficult problem. Finally we robustly tested our original treatments, comparing their efficacy using these assessments.

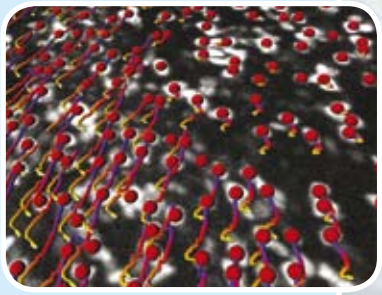
One of the difficulties for many previous researchers in this area has been how to selectively target and dampen adhesions without causing impaired tissue repair. We found that our new treatments have highly significant adhesion cell blocking effects and may even promote healing.

One other drawback of previously tested treatments is their acceptability to patients. We have investigated a number of treatments, which although plant-derived, are both powerful and acceptable.

These results are new and exciting and will enable progress to be made in this area of surgery, which has broad application and direct clinical relevance. We are currently further developing these novel treatments and are comparing them with others that have had variable success. If successful this work will lead directly to clinical trials to improve patient outcomes.

Adhesions may lead to permanent disability, debilitating pain, infertility, bowel obstruction and death. Further surgery to correct adhesions is often unsuccessful and acts as a stimulus for further adhesion formation, making this a very difficult problem to solve.

Such treatments may dramatically reduce this debilitating and dangerous consequence of many surgical procedures.



Digital image of adhesion tissue cells showing how they respond dynamically to stress.

Fellowship/Sponsor
RCS Research Fellowship

Mr Olivier Branford

Site of study
RAFT Institute of Plastic Surgery, Mount Vernon Hospital, Middlesex

Further funding
The Community Fund National Lottery Research Grant (£117,000) 2004–2006
Rosetrees Trust Research Grant (£3,000) 2005

Supervisors
Mr Adriaan O Grobbelaar

Presentations

The British Association of Plastic Surgeons, London, Royal College of Surgeons, November 2005

The 11th Congress of the Federation of the European Societies for Surgery of the Hand, Glasgow, June 2006

Olivier with research supervisor Adriaan Grobbelaar retrieving adhesion tissue samples from cryopreservation at RAFT.

using microdialysis
to monitor deep burn wounds

Fellowship/Sponsor
Royal College of Surgeons
One-Year Research Fellowship

Miss Eleonore Breuning

Site of study
Burns Unit, University Hospital Birmingham

Further funding
British Association of Plastic Reconstructive and Aesthetic Surgeons: Paton/Masser Award

The Association of Clinical Biochemists, West Midlands region: Robert Gaddie Memorial Award

West Midlands Regional Burn Unit Trust Fund (two years)

Supervisors
Naiem Moiemen
Peter Gosling

Presentations

Caribbean College of Surgeons 5th Annual Scientific Meeting, St Lucia, June 2007

4th International Conference on Clinical Microdialysis, Cambridge, September 2007

Prizes

Best Paper, Caribbean College of Surgeons 5th Annual Scientific Meeting

Investigation of dermal metabolism in burned and unburned human skin

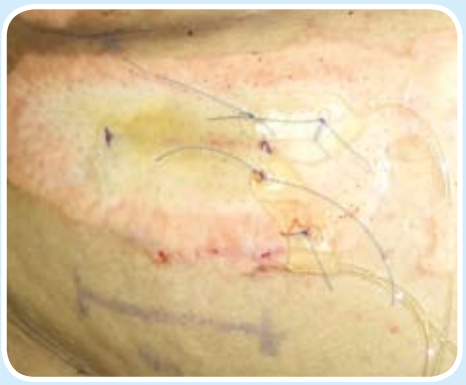
Deep burns cause disfiguring and disabling scars. Burns can progress to become deeper and larger than the original injury if conditions are unfavourable in the first few days. At present there is no way of monitoring the burn wound to ensure that conditions are good. The aim of this project was to investigate a potential method of monitoring the burn wound, to improve our understanding of the changes which lead to its progression. In the future we hope to use this monitoring to optimise treatment of the patient and minimise scarring.

The project consisted of three separate studies, each using a technique called microdialysis. This involves insertion of a small probe into the skin or wound, allowing collection of tiny samples of fluid from around the cells. Analysing this fluid allows us to see how the cells respond to their environment, and adverse changes can be identified before permanent damage arises.

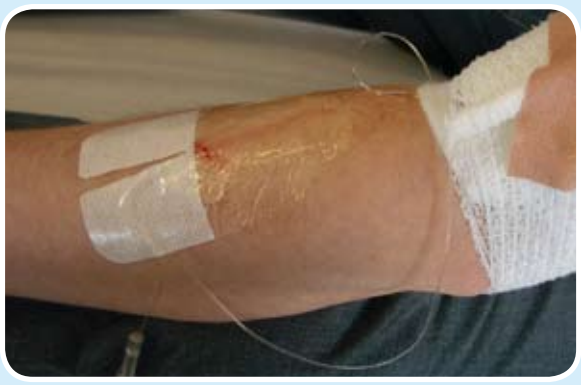
The first study investigated the skin of 10 healthy volunteers to establish a set of normal values for this technique. The second study involved inserting probes into the centre and edge of the wound and into unburned skin of patients with burns covering less than 15% of their body. Samples of fluid from these three areas were analysed to establish patterns of behaviour of these three zones over the first 36 hours following injury. A third study will look at the behaviour of burn wounds which cover more than 15% of the body.

Several interesting trends have been found, with distinct patterns for different areas within the burn. Additional experiments are being performed to confirm whether these changes are caused by the injured cells themselves or the environment surrounding them. Further research can then be undertaken to test whether manipulating the wound environment translates to a reduction in scarring.

'Over 10,000 patients are admitted to hospital with burns each year.'



Burn wound with microdialysis probes in situ.



Volunteer undergoing microdialysis of normal skin.

assessing
patient features to lower risk of stroke in surgery

A Comparison of the sub-clinical effects of carotid endarterectomy and carotid artery stenting

Traditional open surgery and newer, minimally invasive techniques can treat narrowed arteries that supply the brain with blood and thereby reduce the risk of future stroke. While they are equivalent in terms of the risk of causing a stroke during the procedure, we wanted to investigate the sub-clinical (or hidden) effects on the brain.

We closely studied more than 50 patients undergoing these procedures. We looked at changes in blood flow to the brain during and after surgery, and assessed changes in how well the brain functions after surgery using special tests of learning, memory and practical tasks. We also worked very closely with specialist companies to use blood tests that are able to identify very minor levels of brain injury not usually detected by examining patients.

Both techniques offer very acceptable results in terms of stroke prevention. However, each technique can injure the brain but via slightly different mechanisms that we are still investigating further. Each technique is very effective at restoring near-normal blood flow to the brain, but we have been able to identify features in patients that may not let this happen. Our work has enabled a greater understanding and application of blood tests that can identify hidden brain injury.

Our department has a long history of research into this disease and surgery for treating it. We hope that using samples collected over a long period we can overlap this work further, enabling greater insight. Ultimately we want to be able to assess a patient, his or her disease, and his or her brain and its blood supply or order to offer a *personalised* operation that carries the greatest chance of a successful outcome.

There has been limited research into this area; ours is the most in-depth study to date. This work has many important 'spin-offs', such as the use of blood tests to predict the risk of stroke after other vascular and non-vascular operations. The work will continue to develop under my supervision.

Patients who suffer a post-operative stroke are universally left disabled to a lesser or greater degree. Some may only experience mild weakness in a limb for example, while others are left completely dependent on others for their care.

Reducing all forms of brain injury during surgery will greatly help patients maintain their independence and quality of life – even if this means still being able to complete a crossword or remember where the front door keys are, rather than just preventing life-changing strokes.

'Up to 40% of strokes can be prevented with surgery on the main arteries supplying the brain.'

Fellowship/Sponsor
Joint RCS England/Stroke Association Fellowship

Mr Robert Brightwell

Site of study
Imperial College, St Mary's Hospital Campus, Paddington, London

Further funding
Industrial collaborators for 18 months

Supervisors
Professor NJW Cheshire

Publications

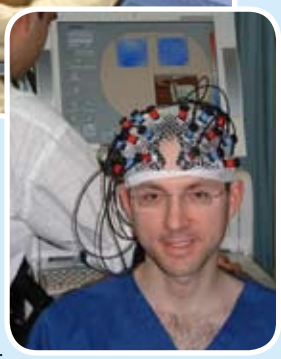
Brightwell RE, Sherwood RA, Athanasiou T, Hamady M, and Cheshire NJW. The Neurological Morbidity of Carotid Revascularisation: Using Markers of Cellular Brain Injury to Compare CEA and CAS. *Eur J Vasc Endovasc Surg* 2007:**34**(5);552-560

Presentations

Charing Cross Symposium, Imperial College, London, April, 2005

European Congress of Radiology, Vienna, March, 2007

Professor Cheshire and Dr Hamady at St Mary's Hospital placing a stent in a patient's right internal carotid artery.



Rob undertaking research in the laboratory at The Academic Surgical Unit, St Mary's Hospital.

defining the processes
responsible for aneurysm rupture

Fellowship/Sponsor
Cazenove Charitable Trust
and Rosetrees Trust

Mr Edward Choke

Site of study
St George's, University of London

Further funding
SARS academic research bursary (one year)
Peel Medical Research Trust (one year)

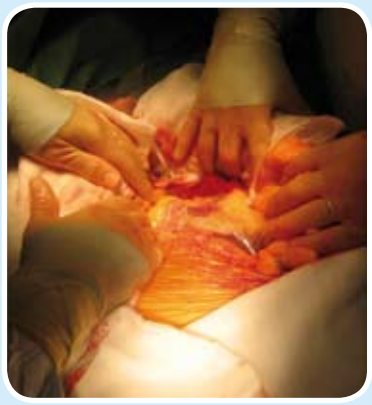
Supervisors
Professor Matt Thompson
Dr Gillian Cockerill

Publications
Arterioscler Thromb Vasc Biol. 2006 Sep;**26**(9):2077–82
Ann N Y Acad Sci. 2006 Nov;**1085**:311–4

Presentations
American Heart Association Scientific Sessions, Dallas, November 2005
Society of Academic and Research Surgery Annual Conference, Cambridge, January 2007

Prizes
ATVB Merit Award for Young Investigators, American Heart Association, November 2005
MRS Young Investigator Award 3rd Prize, Medical Research Society and Royal College of Physicians, London, February 2007


Ed in Hong Kong, RCS Triennial trip, Voyage of the Eagle.


Emergency operation for ruptured abdominal aortic aneurysm.

Molecular mechanisms of abdominal aortic aneurysm rupture

Aneurysms are localised bulges in blood vessels caused by vessel wall weakness. Abdominal aortic aneurysms (AAA) primarily affect elderly males with a prevalence of 5%. The natural history of aneurysms is expansion and eventual rupture, often with fatal consequences. The bigger the aneurysm, the more likely it is to rupture. AAA rupture is the 13th commonest cause of death in the Western world. The processes underlying aneurysm rupture remain poorly defined and currently there is no pharmacological treatment available to prevent it.

This project aimed to define the processes responsible for aneurysm rupture. Previous studies showed that within an aneurysm, there were discrete microenvironments of altered biological activity that gave rise to areas of weakened aneurysm wall that might predispose to rupture. In this project, we compared tissues from the site of aneurysm rupture to a non-ruptured area of the same aneurysm and demonstrated increased new blood vessel formation (angiogenesis) at the site of aneurysm rupture. The significance of this finding is that the mandatory expression of proteolytic enzymes during such angiogenic response may have caused aneurysm rupture by weakening the vessel wall.

In addition, we used microarray gene expression technology to identify novel gene pathways involved in aneurysm rupture. This technique demonstrated that key pro-angiogenic genes were overexpressed at the aneurysm rupture site, the most interesting of which was vascular endothelial growth factor (VEGF). Other genes identified were those involved in immune response, inflammatory response and cell death. Using experimental aneurysm models, we then showed that VEGF treatment led to earlier formation of aneurysms, which were significantly more severe and larger than non-treated control groups.

Data from this project have provided a reference framework for the development of protective strategies specifically targeted at preventing aneurysm rupture. Future work will test whether anti-angiogenic therapy reduces risk of aneurysm rupture.

'Aneurysm rupture is responsible for 1.5% of the total mortality in males over 55 years of age and in England, aneurysms cause 8,000 deaths per year.'

understanding
how mouth cancer cells spread

Jonathan receives the Hatton Prize from the president and research director of the International Association for Dental Research.

Chemokine receptor profiles in metastatic oral squamous cell carcinoma in-vivo

Cancer of the mouth is a disabling and often fatal condition. Treatment frequently involves disfiguring surgery that affects not only facial appearance, but also fundamental functions such as eating and speaking. Spread of cancer cells to the lymph glands of the neck is common and requires treatment including further surgery and radiotherapy. The aim of this project was to improve our understanding of how mouth cancer cells spread (metastasise) and, in the long run, help develop and target treatments to remove the cancer cells while minimising the impact on the patient's everyday appearance and activities.

'Mouth cancer is seldom talked about but is the sixth most common cancer worldwide.'

Reports from the literature suggested that cell surface proteins (called chemokine receptors) were associated with cancer metastasis in tumours of the breast, lung and stomach. My work was the first to investigate these proteins in mouth cancer cells growing in the laboratory. The results showed that tumour cells (that had been manipulated in the laboratory to produce high levels of specific chemokine receptors) were more likely to invade, grow and spread than untreated controls. Furthermore, in clinical samples taken for pathology, high levels of these receptors were associated with the presence of lymph gland metastasis. These findings suggest that chemokine receptors are implicated in spread of cancers of the mouth. Further preliminary investigations are being carried to determine if this molecular pathway might offer a potential target for new therapies against mouth cancer. It is also possible that by identifying these molecules in patient samples surgeons may get a better guide as to whether the cancers they are seeing have covertly spread to the lymph glands.

Fellowship/Sponsor

Frances & Augustus Newman Foundation Surgical Research Fellowship

Mr Jonathan Collier

Site of study

Institute of cell and molecular science, Barts and The London School of Medicine and Dentistry, Queen Mary University London

Further funding

Cancer Research UK and Queen Mary University London Research Advisory Board (two years)

Supervisors

Dr Ahmed Waseem

Presentations

International Association of Dental Research Annual Scientific Congress 2006, Brisbane, 2006

International Congress on Oral Cancer 2005, Crete, 2006

Prizes

International Association for Dental Research, Hatton Award, 2006

British Association of Dental Research, Colgate Prize, 2006

Jonathan examines immunohistochemical staining of patient tissue arrays.

new treatments
to prevent and treat bowel cancers

Fellowship/Sponsor
RCS/WOMAC (1 year)
and RCS/SARS (year 2/3)

Mr John Conti

Site of study
University of Southampton

Further funding
RCS/SARS fellowship and Wessex Cancer Trust, for additional consumable funding

Supervisors
Professor JN Primrose
Professor JP Iredale

Publications
Clinical Cancer Research, 2004;**10**: 7427–37

Presentations
The Annual meeting of the American Association of Cancer Research (AACR), March 2004

The Annual meeting of the American Association of Cancer Research (AACR), April 2005

Prizes
MRS oral presentation plenary session 1st prize, The Medical Research Society (MRS), 2003

Best talk prize, Wessex Surgeons meeting, 2004

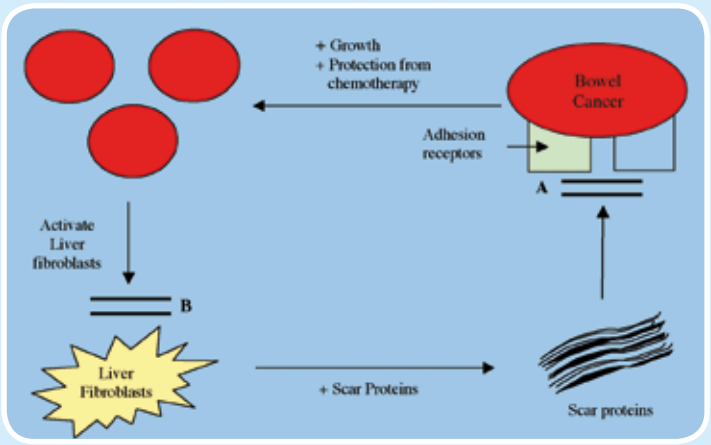
The facilitative role of the extracellular matrix in the development of colorectal cancer liver metastases

Cells, whether they are normal or cancerous, do not survive in isolation and how these cells interact with proteins that surround them (the matrix) can profoundly influence the growth of both normal and cancerous cells. In response to cutting the skin the body responds to heal the damage by producing scar proteins to close the defect. We have been able to demonstrate that a similar process occurs within the liver when it is seeded by bowel cancer cells. It would be easy to assume that the production of scar proteins would help to slow down the growth of the cancer. However, our work has suggested that bowel cancer cells grow faster on scar proteins and when the cancer cells are treated with chemotherapy (which aims to destroy cancer cells) being in contact with the scar proteins protects the cancer cells from the toxic effects of chemotherapy.

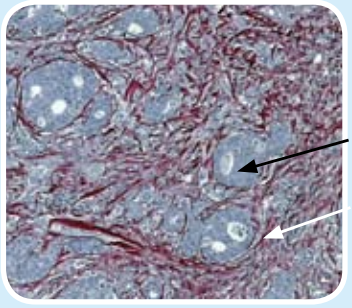
We have demonstrated the importance of cancer cell expression of specific adhesion molecules, which enables the cancer cells to stick to scar proteins. By blocking these adhesion molecules the beneficial growth effects for cancer cells grown on scar proteins are ablated. We have also demonstrated that the scar proteins are predominantly produced by our own resident liver cells (liver fibroblasts) rather than the cancer cells themselves. By encouraging the body's natural response to injury the cancer cells can promote the production of beneficial scar proteins and thrive. The effects of scar proteins on bowel cancer cell growth are illustrated in figure 1. In addition this figure illustrates where exciting new opportunities may exist to help treat and prevent the development of liver metastases in patients with bowel cancer or make our present treatments more effective, eg chemotherapy.

These studies are ongoing and potentially offer the hope of novel new treatment options for patients with bowel cancer.

'Bowel cancer is the second commonest cause of death from cancer in the UK. The spread of bowel cancer to involve the liver (liver metastases) is a major cause of death from this disease.'



The role of scar proteins in encouraging cancer cell growth and where possible new treatments could be targeted by either blocking the cancer cells binding to the scar proteins (A), by the use of drugs which block the adhesion molecules, thereby preventing the cancer cells sticking to scar proteins or by preventing the liver cells producing scar proteins (B).



This image illustrates how the bowel cancer cells (stained blue – black arrows) that have spread to the liver are surrounded by scar proteins (stained red – white arrows).

seeking
better clinical therapies for CDH

Endothelial-vascular smooth muscle interactions in the hypertensive hypoplastic perinatal lung

Congenital diaphragmatic hernia (CDH) is a common birth defect of unknown aetiology, with mortality nearing 50%. Babies with CDH have a diaphragmatic defect, such that the intestines lie in the chest and, critically, they have abnormal lungs. Affected babies die, despite modern intensive therapy, from inadequate lungs that are prone to poor oxygenation and pulmonary hypertension (PHT). Survivors have variable quality of life, depending upon lung function and co-existing abnormalities. Severely affected survivors have high morbidity including oxygen dependence, feeding disorders and poor growth. Seeking better clinical therapies for CDH will hopefully impact on severity of chronic lung disease and improve quality of life for survivors.

PHT is also a fatal adult disease. Recently, a gene was identified in patients with PHT (bmpr2) and abnormalities detected in proteins from associated biochemical pathways. This research aimed to investigate these abnormal proteins in CDH, to seek a potentially treatable biochemical abnormality that could improve survival. Additional studies examined a critical cell signalling system (phospho-proteins) for aberrations.

The studies used lung from an experimental model of CDH. The experiments looked at the levels of proteins linked to adult PHT. The cell-signalling studies utilised a combination of biochemical methods, culminating in identification of unknown proteins by mass spectrometry.

The signalling proteins that are deranged in adult pulmonary hypertension were normal in this model of CDH. These data indicate that PHT in CDH has a different mechanism to adult PHT, and may require distinct treatments. However, these proteins are developmentally regulated, suggesting an important role in adaption at birth. The phospho-protein data found that two proteins are more activated in CDH lung. On going studies aim to characterise these proteins and their role in CDH pathophysiology.

This is an active research field in the effort to develop new therapies for CDH. This work represents an exciting new development in understanding the molecular biology of PHT in CDH. The Liverpool-based academic paediatric surgery group remain the leading UK team researching this field.

Harriet operating at Alder Hey Children's Hospital, Liverpool.

Professor Losty and Harriet discuss a Western blot of lung phospho-proteins.

'Despite modern neonatal intensive care, up to half of all babies with congenital diaphragmatic hernia die from poor lung growth and high blood pressure in the lungs.'

Fellowship/Sponsor
MRC/Royal College of Surgeons of England Clinical Research Fellow

Miss Harriet Corbett

Site of study
School of Biological Sciences and Division of Child Health, University of Liverpool

Further funding
Birth Defects Foundation (six months)

Supervisors
Professor Paul Losty
Mr Edwin Jesudason

Publications

Pediatr Surg Int. **22**: 95–98, 2006

Paediatric Thoracic Surgery. 1st Edition. In press, 2008

Presentations

American Thoracic Society, San Francisco, May 2007

British Thoracic Society winter meeting, London, December 2006

Prizes

Medical Research Council clinical training fellowship 2004-2007 (joint MRC/RCS award)

studies contributing
to drug treatment development for aneurysms

Fellowship/Sponsor
The Freemasons

Mr Joseph Dawson

Site of study
St George's Vascular Institute,
St George's University of London

Further funding
The Peel Medical Research Trust Grant 2006 (one-off payment)

Supervisors
Professor Matt Thompson

Publications
J Vasc Surgery 2007; **45**(2):350–6

Curr Vasc Pharmacol 2006; **4**(2): 129–149

Presentations
New York Academy of Science, Columbia University, New York, April 2006

Cardiovascular and Interventional Radiology Society of Europe, Rome, September 2006

Prizes
Society of Academic and Research Surgery President's Prize, 2007

The Peel Medical Research Trust Grant, 2006

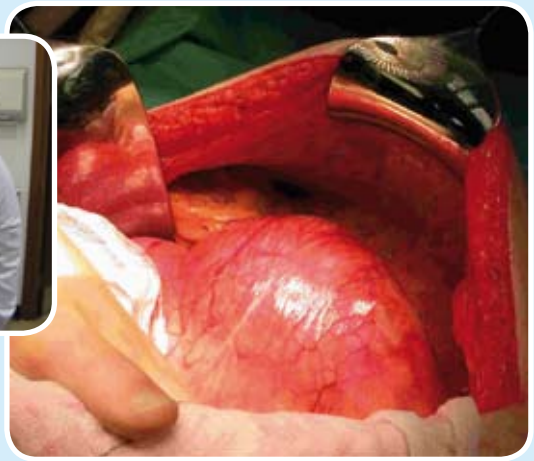
The role of lipid lowering in abdominal aortic aneurysms

Abdominal aortic aneurysms (AAA) are slow-growing swellings of the main artery within the abdomen. If untreated they ultimately rupture which is usually fatal. Surgery is suitable for those with large AAA but there is currently no treatment for small aneurysms. The aim of this research was to advance the development of drug treatment of aneurysms and the approach was two-fold; to expand our knowledge regarding certain factors thought to influence AAA growth and to carry out a trial to study the effect of cholesterol-lowering drugs on aneurysm expansion.

Interleukin-6 (IL-6) is an inflammatory molecule linked to aneurysm growth, with previous studies identifying higher levels in patients with AAA. Elevated IL-6 is linked to heart attacks, and we wanted to determine whether it is the aneurysm itself that actually produces IL-6. By measuring IL-6 directly from inside the aorta using keyhole techniques we have shown that the aneurysm 'leaks' IL-6 into the circulation. We then focused our attention on endothelial progenitor cells (EPCs), a potentially important stem cell not previous studied in AAA. We found that there was almost twice the number of EPCs in patients with AAA compared to those without. With further research EPCs may provide a future drug target in the treatment of AAA.

Previous studies have suggested that cholesterol-lowering drugs (statins) reduce the growth of AAA by reducing, amongst other things, IL-6. We looked at whether reducing cholesterol even further with a combination of cholesterol-lowing drugs reduced AAA growth. We showed that the combination therapy reduced factors in the blood linked to aneurysm growth, including IL-6. These results would support a large trial studying cholesterol-lowering on aneurysm growth rates and suggests that there may be a role in the medical treatment of AAA using these drugs.

Joseph working in the laboratory.



An Abdominal Aortic Aneurysm: a swelling of the main artery in the abdomen. (ref: www.endologix.com).

'The overall mortality following rupture of an abdominal aortic aneurysm is approximately 80%, accounting for 10,000 deaths annually in the UK. Up to 10% of men over 65 are affected, but aneurysms often cause no symptoms and currently there is no treatment for small aneurysms.'

'In a study of oral mucosal and patient-matched skin fibroblasts, clear inherent differences were observed in the behavioural patterns of the fibroblasts, which have helped explain scarless healing in the oral mucosa and scar formation in the skin.'

Phenotypic and genotypic characterisation of oral mucosal and patient-matched skin fibroblasts

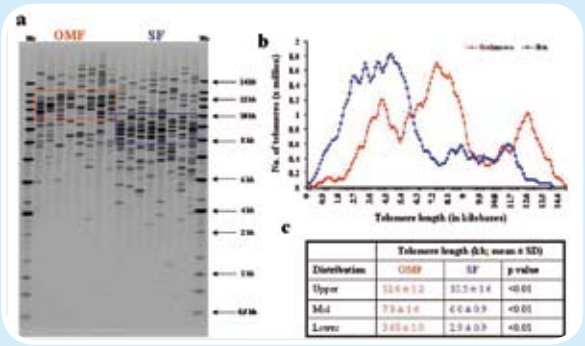
Burn injuries continue to remain a serious cause of morbidity and mortality globally. They result in varying degrees of scarring depending on the depth and severity. Contractures, a variant of scar, arising from burn injuries can result in severe functional difficulties. Excessively scarring conditions such as hypertrophic and keloid scars can further exacerbate the problem. In contrast to skin, oral mucosal wounds heal rapidly and in a scarless fashion. Contractures, hypertrophic or keloid scars are not seen in the oral mucosa.

Fibroblasts are cells that play crucial roles in various stages of wound healing. The aims of my research were to evaluate the phenotypic characteristics, ageing profiles, pattern of gene transcription and phenotypic responses between oral mucosal fibroblasts (OMF) and skin fibroblasts (SF) in an attempt to explain their differential wound healing outcomes.

Methods: Patient-matched oral buccal mucosal and skin fibroblasts were obtained (n=4). The cells were cultured until senescence. Various cellular, molecular and gene transcription experiments were undertaken both during the proliferative phase and at senescence.

Results: Compared to SF, OMF underwent more population doublings ('lived' longer) and senesced later. Throughout proliferation, the OMF had higher proportion of longer telomeres ('markers of ageing'). Multipotent stem cells were identified only among OMF. Gene transcription analysis of thousands of genes identified differential regulation of numerous genes between SF and OMF. The differences in ageing profiles and gene transcription were complemented by the increased ability of OMF to repopulate in-vitro monolayer wounds and reorganise their surrounding extracellular matrix environment throughout propagation.

Discussion and future directions: The identification of multipotent stem cells in oral mucosa has direct in-vivo clinical application in the fields of tissue engineering, tissue repair and regeneration. The genes and pathways can be targeted for up-or down-regulating the gene expression in-vitro, which will form the basis for gene manipulation in-vivo. The results of this research have formed the basis for developing future therapeutic targets aimed at ameliorating scarring and burn contractures.



Measuring the individual telomere lengths to delineate the ageing profiles (a) Oral mucosal fibroblasts (red) have longer telomeres than skin fibroblasts (blue) (b & c) Histogram & table demonstrating the telomere lengths.

Fellowship/Sponsor

RCS England Surgical Research Fellowship

Mr Stuart Enoch

Site of study

Cardiff University

Further funding

Joint Royal Colleges of Surgeons of Edinburgh and Ireland (2004–2005) (9 months)

Supervisors

Dr Phil Stephens
Professor David Thomas

Publications

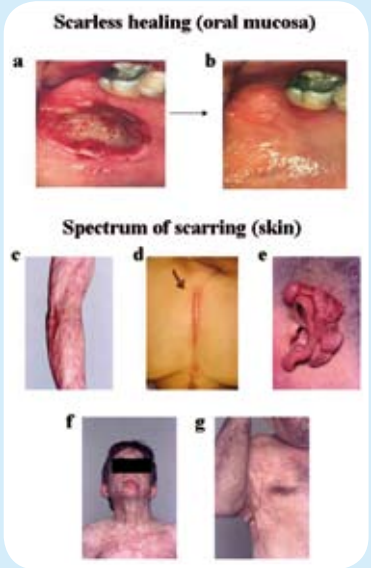
Surgery 2005; **23**(2): 37-42.

European Tissue Repair Society News Bulletin, 2006; **13**(3&4): 54-55

Prizes

Burns and Plastic Surgery award (Wounds UK), London, June 2007

Young Investigator Award, The European Tissue Repair Society, Pisa, September 2006



Differential wound healing in oral mucosa and skin (a & b) Healing in oral mucosa without scar formation (c) Burn scar (d) Hypertrophic scar (e) Keloid scar (f & g) Severe contractures due to burns.

providing evidence that
adhesions are dynamic vascular structures

Fellowship/Sponsor
Cazenove Fellowship

Mr Jonathan Epstein

Site of study
University of Manchester and Christie Hospital, Manchester

Supervisors
Mr MS Wilson
Dr SE Herrick

Publications
Diseases of the Colon & Rectum 2006 **49**(12) 1,885–92

Adhesions News & Views 2006 9 p20–22

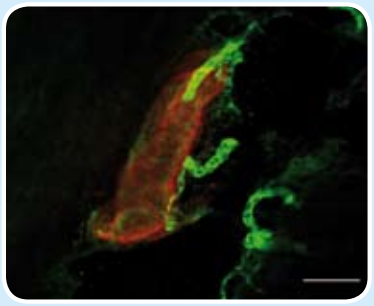
Presentations
Association of Surgeons of Great Britain and Ireland, Glasgow, 2005

Association of Coloproctology of Great Britain and Ireland, Gateshead, 2006

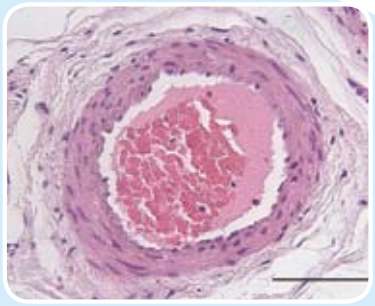
Prizes
Best Poster Prize, Tripartite Colorectal Meeting, Dublin, 2005

Best Presentation Prize, VIIth PAX Meeting, Leuven, 2006

Jonathan at work.



Section through a human adhesion which demonstrates a blood vessel (haematoxylin & eosin, bar = 50µm).



A thick section through a human adhesion immunostained for vascular markers demonstrates a three-dimensional vascular network (bar = 50µm).

The role of angiogenesis in peritoneal adhesion formation and persistence

Peritoneal adhesions are abnormal bands of tissue, which form between abdominal organs after surgery. Adhesions are found in up to 95% of patients after abdominal surgery and can lead to significant symptoms. Adhesions are the most common cause of small bowel obstruction in the developed world, which can result in pain, hospital admission and often further surgery. Adhesions are also a common cause of female infertility, are linked to chronic pain and add to the difficulty and danger of abdominal surgery.

The basic processes leading to adhesion formation are incompletely defined. Angiogenesis, the development of a blood supply, is known to be important in the progression of many diseases but little is known about the vascular structure of adhesions and what role angiogenesis plays in adhesion formation.

In the first part of this project we found that blood vessels could be seen in thin slices of human adhesions examined under the microscope. These adhesion vessels were shown to contain characteristic markers, which identify normal blood vessels and also to contain growth-promoting agents known to be involved in new blood vessel development. A laser microscope was used to take three-dimensional images, which revealed that blood vessels in adhesions formed complex branching networks comparable to those found in healing skin wounds.

'Nearly 95% of patients form adhesions after abdominal surgery.'

In the second part of the project we developed an animal model of adhesion formation after surgery. We found that these adhesions formed blood vessels and expressed the same growth-promoting agent found in human adhesions. An antibody designed to block blood vessel formation by this growth promoter led to a significant reduction in adhesion formation in the animal model.

This study provides strong evidence that adhesions are dynamic, vascular structures not merely inert scar tissue as has previously been thought. These results also suggest that drugs, which block blood vessel growth, have the potential to prevent adhesion formation and reduce the associated disease burden.

identifying structural and nerve problems causing constipation

Constipation: detailed investigation allows improved selection of patients for surgery

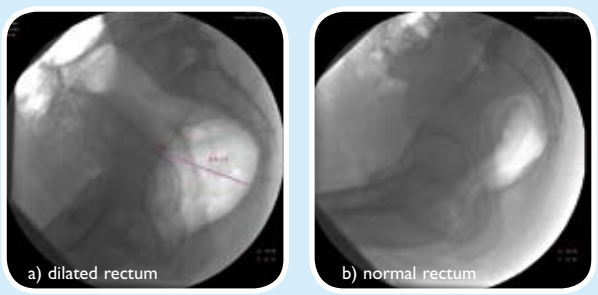
The management of patients with intractable constipation who fail to respond to non-surgical intervention is a difficult challenge for coloproctologists. Functional constipation is common, affecting up to 10% of the population, causes considerable suffering and has a major impact on quality of life.

Identification of the underlying reasons why patients become constipated is crucial to successful management. Commonly, such patients lose rectal sensation leading to loss of the awareness of the need to defaecate and are said to have rectal hyposensitivity. Additionally, a proportion of constipated patients develop gross dilation of the rectum, which is termed idiopathic megarectum.

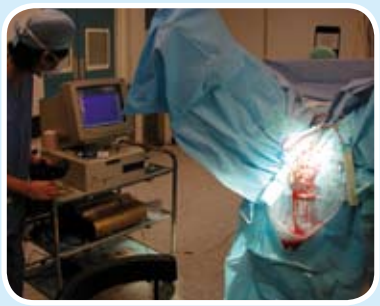
The aims of my research project were to (i) determine whether loss of rectal sensation in constipated patients was due to (a) abnormalities of the structure of rectum or (b) impaired nerve signalling between the rectum and the brain and spinal cord, and (ii) evaluate surgical strategies in constipated patients with dilatation of the rectum (megarectum).

Patients with constipation were compared to age-and sex-matched healthy volunteers. All subjects underwent measurement of rectal diameter, elasticity (compliance) and sensitivity using advanced anorectal physiological investigations, including barostat studies and thermal and electrical stimulation of the rectal mucosa to assess nerve signalling from the rectum. Such investigations revealed that two-thirds of patients with loss of rectal sensation had abnormal rectal structure rather than nerve signalling problems. Accordingly, a novel surgical procedure, vertical reduction rectoplasty, which was pioneered to reduce rectal capacity and thus restore rectal sensation, was performed in these patients. At 5 years after surgery, the procedure was effective in 8 of 10 patients.

Following this initial work, further studies were performed to investigate the nature and causes of the structural and nerve problems in patients with constipation, and I was inspired to complete a PhD thesis related to this topic. Completion of the project also stimulated my desire to pursue a career as an academic surgeon, and I have recently been successful in being appointed to one of the UKCRC Clinical Lectureships in Surgery.



Rectal size in constipated patients. Image (a) shows dilation of the rectum compared with an asymptomatic subject (image b). This patient had normal nerve signalling and was thus suitable to undergo surgical correction of the dilated rectum.



The use of the rectal barostat in the operating theatre to allow reduction of rectal size to a pre-determined volume and pressure.

'In 2 of 3 constipated patients, loss of rectal sensation was due to dilatation of the rectum rather than problems with nerve signalling, making them suitable for surgical intervention.'

Fellowship/Sponsor

The Frances and Augustus Newman Foundation Research Fellowship

Mr Marc A Gladman

Site of study

Centre for Academic Surgery, Bart's and The London, Queen Mary's School of Medicine & Dentistry, London UK

Further funding

Higher Education Funding Council for England (HEFCE) (two years)

Supervisors

Mrs Peter J Lunniss
Professor Norman S Williams

Publications

Am J Gastroenterol 2005; **100**: 106–114

Br J Surg 2005; **92**: 624–630

Presentations

The American Gastroenterological Association Annual meeting, Digestive Disease Week 2007, Washington DC, May 2007

The Association of Coloproctology of Great Britain and Ireland, Birmingham, July 2004

developing a method
of accelerating thrombus resolution

Fellowship/Sponsor
Enid Linder Foundation
and Rosetrees Trust

Mr James Gossage

Site of study
Academic Department of Surgery,
St Thomas' Hospital

Supervisors
Dr Alberto Smith

Publications
Journal of Vascular Surgery 2006; **44**: 1,085–90

Presentations
SARS Patey prize session, Edinburgh, January 2006
American Venous Forum, Miami, February 2006

Prizes
Hunterian Professorship, 2007

'The incidence of deep venous thrombosis in the general population is about 0.05% per annum with one in every three patients developing post-thrombotic complications within five years.'

Enhancing fibrinolysis to promote venous thrombus resolution

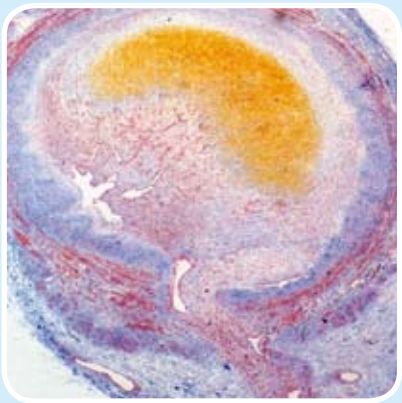
Blood clots can form in the deep veins of the leg leading to a condition known as deep vein thrombosis (DVT). In the UK approximately 5 people per 10,000 are diagnosed with this condition each year. Within five years, one in three patients will develop a condition known as post-thrombotic syndrome, consisting of pain, swelling and leg ulceration. It is a major cause of chronic ill health in the general population and is a burden for the NHS.

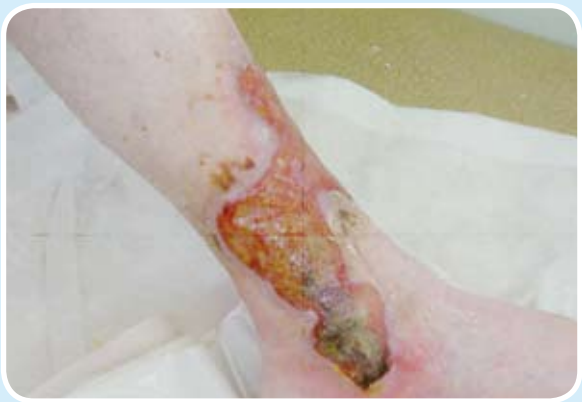
Rapid natural thrombus resolution is associated with reduced vein damage and a lower incidence of the post-thrombotic syndrome. The aim of the study was to develop a method of accelerating thrombus resolution, without the risks of bleeding associated with current treatments.

Urokinase is a naturally occurring enzyme that is known to be important in thrombus resolution. A virus, carrying the gene encoding for urokinase, was used to increase the levels of this enzyme within naturally formed thrombus. This resulted in a 50% reduction in thrombus volume after one week.

Previous work at our institution has shown that a large number of inflammatory cells (monocytes) are recruited into the thrombus during resolution. The second aim of our study was to see if it was possible to use these cells to carry urokinase into the thrombus. Urokinase production was increased in human monocytes by treating them with the virus carrying the urokinase gene construct. The infected cells were then injected into the circulation and shown to migrate into thrombus and cause a significant reduction in its size.

Ideally, monocytes would be treated while they are still in the circulation by targeting specific receptors on the cell surface. A combination of genes could also be transferred into the cells, enhancing their efficacy. This work is to be continued with further support from the British Heart Foundation.


Cross Section of a venous thrombus.


Venous ulceration.

understanding
how genes influence Crohn's disease severity

Laura in the laboratory at The Wellcome Trust Centre for Human Genetics, Oxford.

Clinical and molecular characteristics of isolated colonic Crohn's disease

Crohn's disease is a chronic inflammatory disease which can affect any part of the intestine. It can vary in both disease location and behaviour and lead to a large number of debilitating symptoms such as frequent bowel motions, weight loss, abdominal pain, fatigue and recurrent admissions to hospital for intensive medical treatment or surgery.

Although much is known about the clinical features, the exact cause and mechanism of Crohn's disease is not known. We believe that the development of this form of inflammation of the gut is the result of a combination of genetic factors and environmental factors, including bacteria.

Studies of families and twins have provided compelling evidence for the involvement of genes in the development of Crohn's disease. When Crohn's disease affects the colon only, patients have clinical, genetic and immunological features that are different from those possessed by patients who only have small intestinal disease. This study explored the clinical and genetic characteristics of isolated colonic Crohn's disease and examined whether genes influence disease severity.

A case-control candidate gene association study was performed in which the frequencies of variants (polymorphisms) in candidate genes – genes encoding proteins believed to be involved in disease pathogenesis – were compared in patients and matched healthy controls.

We confirmed the association with an HLA (human leucocyte antigen) gene on chromosome 6 and isolated colonic Crohn's disease. We further demonstrated that these genetic variants predict a severe disease course requiring surgery.

The ultimate goal of these investigations is to individualise patient care based on a genetic profile, providing accurate information for diagnosis, prognosis and treatment. Eventually this may be used in the clinical setting to counsel the patient about the prospect of the increased risk of surgery and will therefore aid the early and appropriate introduction to surgeons and stoma nurses.

Fellowship/Sponsor
The Donald Currie Research Fellowship into Crohn's disease supported by ia

Miss Laura Hancock

Site of study
The Wellcome Trust Centre For Human Genetics, University of Oxford

Supervisors
Professor Neil Mortensen
Professor Derek Jewell
Dr Bryan Warren

Publications

Colorectal Dis. 2006; **1**:10–4

Inflamm Bowel Dis. 2007;**13**(8):941–6

Presentations

The American Gastroenterological Association, Los Angeles, May 2006

The Association of Coloproctology Great Britain and Ireland Annual Meeting, Glasgow, July 2007

Prizes

The Pathological Society of Great Britain and Ireland Travelling Fellowship

The Bowel Disease Research Foundation (BDRF) Research Fellowship

'The ultimate goal of these investigations is to individualise patient care based on a genetic profile, providing accurate information for diagnosis, prognosis and treatment.'

aiming to improve
skin graft processes and healing

Fellowship/Sponsor
Freemasons Surgical Research Fellowship with support from the Rosetrees Trust

Miss Caroline Harrison

Site of study
Clinical Sciences (North), School of Medicine, University of Sheffield

Supervisors
Professor Sheila MacNeil

Publications

Tissue Engineering 2006; **12**: 3119–33

British Journal of Dermatology 2006; **154**: 401–410

Presentations

Joint Meeting of the Tissue and Cell Engineering Society (TCES) and British Society for Matrix Biology (BSMB), Bristol, 2004

British Association of Plastic Surgeons (BAPS) Winter Meeting, London 2005

In vitro use of tissue-engineered skin to investigate skin graft contraction

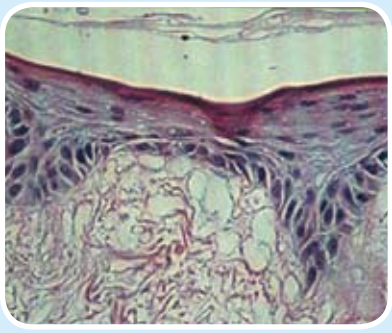
The treatment of patients with extensive burns usually involves large areas of skin grafting. During the healing process these skin grafts contract, causing cosmetic deformities and preventing the full movement of joints. Current approaches to limit contraction involve the patients wearing pressure garments and splints, but often further surgery is needed to release established contractures.

'30% of patients undergoing skin grafting for burns suffer clinically significant graft contracture, with cosmetic deformity and limitation of joint mobility.'

We have developed a tissue-engineered model of skin, based on sterilised human skin and repopulated with cultured human skin cells. This skin composite contracts by up to 60% of its original surface area over 30 days. Using this model, we have gained insights into how skin cells (keratinocytes) contract the underlying skin as they proliferate and mature. We have studied changes in skin collagen synthesis, breakdown and binding during the contraction process and identified some chemical methods to reduce contraction without significantly affecting the appearance and durability of the skin. Eventually, we aim to produce a wound dressing that releases these chemicals directly onto the healing skin graft to attempt to reduce contraction.

We have also studied the way different skin cells (keratinocytes and fibroblasts) interact and have identified differences in this interaction during the different stages of wound healing. In the early stages, the keratinocytes promote synthesis of collagen and other proteins by the fibroblasts, but later, once they have covered the surface of the wound, they act to suppress collagen synthesis. This is consistent with clinical data indicating that prompt coverage of the surface of a wound with skin cells reduces scarring and contraction. We plan to investigate the effect of an extract from screened donor keratinocytes on contraction of tissue-engineered skin in the laboratory, with a view to subsequent progression to clinical studies on grafted burn wounds. Ultimately, we hope to improve the quality of life for patients undergoing skin grafting after major burn injuries.

Contraction of tissue-engineered skin in the laboratory.



The histological appearance of tissue-engineered skin closely resembles normal human skin.

promoting
wider applications for reconstructive surgery

Steps towards reconstructive allotransplantation without immunosuppression

Many people have severe physical defects for which there are limited reconstructive surgery options. Reconstructive transplantation using tissues from other people, including hand and face transplants, have been successful. To promote wider application of these techniques this study is addressing three issues:

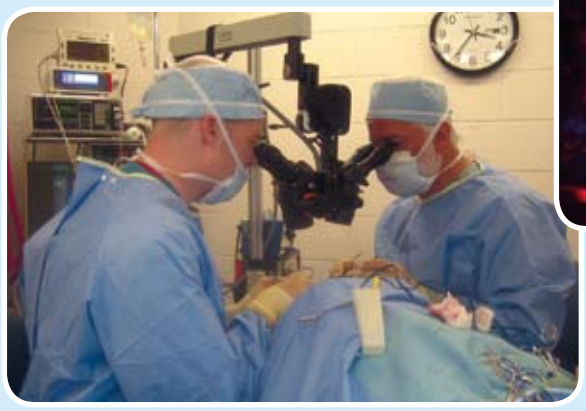
1. In the event of failure of the transplant it is planned to replace it with another one; however, the recipient may be so badly damaged by the failure that it is not possible. This research indicates that it is possible to perform a retransplant and that the retransplant will not be limited in form or function by damage to the recipient.

2. The most likely cause of transplant failure will be rejection of the skin within the transplant by the recipient's immune system. However, the reason why skin is so prone to rejection is not fully understood. Using novel in vivo imaging techniques this study has elucidated skin rejection mechanisms. This has been crucial for developing ways to overcome skin rejection.

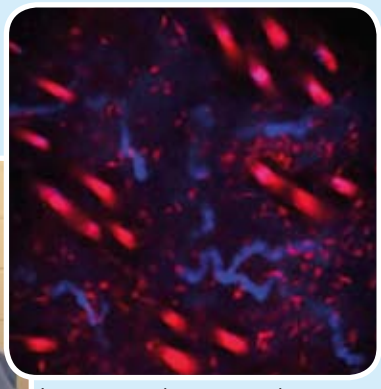
3. At present toxic immunosuppression is required to prevent skin rejection. This research is investigating ways to induce a state in which the recipient would selectively accept the transplant without immunosuppression while still maintaining an otherwise normally functioning immune system. Until now, this has only been possible in small animal models. We have reprogrammed the immune system in a clinically relevant large animal model and are currently testing to see if skin tolerance has been obtained.

The findings of this research have the potential to facilitate the widespread use of reconstructive transplantation techniques and so revolutionise our ability to reconstruct defects which are currently beyond us.

'Each year an estimated 140-million people worldwide sustain severe physical defects for which there are limited reconstructive surgery options.'



Ben performing microsurgical skin flap transplant on an animal model with supervisor Mark Randolph.



In vivo imaging demonstrating the rejecting cells gathering around hair follicles and blood vessels in a skin transplant.

Fellowship/Sponsor
Freemasons Surgical Research Fellowship

Mr Ben Horner

Site of study
London/Boston

Supervisors
Mr Peter EM Butler
Mr Shehan Hettiaratchy
Mr Mark Randolph
Dr Christene Huang

Publications

Am J Transplant. 2006 Dec;6(12):2894-902

Skin Tolerance: In search of the Holy Grail. Provisionally Accepted by *Transplantation International*

Presentations

World Composite Tissue Allotransplantation Symposium, Tucson, 2006

Plastic Surgery Research Council, Stanford University, California, 2007

Prizes

Best Presentation at the World Composite Tissue Allotransplantation Symposium, 2006

studies contributing
to development for spinal cord regeneration

Fellowship/Sponsor
RCS Lang Research Fellowship

Mr Kismet Hossain-Ibrahim PhD

Site of study
University College London

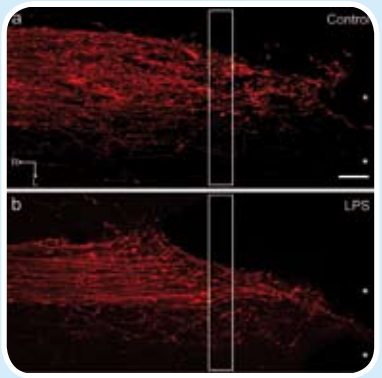
Further funding
Wellcome Trust, UK (three years)

Supervisors
Professor P N Anderson
Professor A R Lieberman

Publications
BMC Neuroscience 2006, **7**: 8
BMC Neuroscience 2007, in press

Presentations
Society of British Neurological Surgeons, Cardiff, 2003
Society for Neuroscience, San Diego, 2004

Prizes
Lang Research Fellowship, Royal College of Surgeons of England, 2005



Horizontal sections of spinal cord with labelled corticospinal axons 21 days after injury. No axons appear to circumnavigate or regenerate beyond the lesion in animals treated with lipolysaccharide (LPS), nor in control animals. * = lesion; R = rostral; L = lateral; bar = 100 µm.

Studies in axonal regeneration in the nervous system

Spinal cord injury is a devastating condition that typically affects the young victims of trauma. Once injured the spinal cord cannot regenerate – unlike the peripheral nervous system (PNS) – due to:
• the poor regenerative response of central nervous system (CNS) cells to injury; and
• the inhibitory nature of the CNS microenvironment.

1. We attempted to stimulate CNS neurons to regenerate by inducing inflammation;
2. We examined the role of NG2 – a major inhibitory molecule of the CNS.

Methods:
1. The inflammatory agent lipolysaccharide was applied to the surface of brain controlling limb movement (motor cortex) and a spinal cord lesion was made at the same time. We examined whether growth associated genes were upregulated in the cell bodies of injured corticospinal neurons and if inflammation around these cell bodies had enhanced axonal regeneration at the injury site.
2. NG2 inhibits axon growth in vitro and is in the scars that form at spinal cord injury sites. We performed various PNS and CNS injuries in NG2 animal model to ascertain whether complete absence of this inhibitory molecule would affect axon regeneration, relative to wild-type controls.

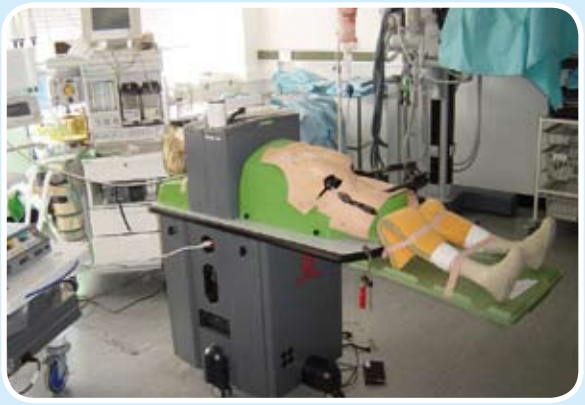
Results:
1. Inflammation caused upregulation of genes in corticospinal neurons known to be associated with successful regeneration in the PNS. However, this stimulation of growth-associated gene expression was insufficient to promote regeneration across a spinal cord lesion.
2. Absence of NG2 did not enhance regeneration of injured ascending or descending axons within the spinal cord tract. Axons in the PNS regenerated and reinnervated peripheral tissues to the same extent and at the same rate in knockout and control groups.

In conclusion inflammation alone is insufficient to promote spinal cord repair and NG2 is not a major inhibitory molecule blocking CNS axon regeneration after injury. Greater understanding of the mechanisms preventing CNS repair through research such as this will help us to stimulate spinal cord repair, and help overcome the lifelong paralysis caused by spinal injuries.

Kismet handling tissue specimens under a dissecting microscope with Professor Patrick Anderson behind and research technician (Gemma Holding) cutting sections on a cryostat in the foreground, UCL.

'Combining inflammation in CNS cell bodies and reducing the CNS inhibitory environment may result in spinal cord regeneration.'

assessing
training methods for surgical judgement



Simulation of keyhole surgery to remove the gallbladder.

Surgical judgment and decision making

Surgeons, in conjunction with their patients and colleagues, have to make risky and irreversible choices. Surgery is often thought of as a craft, but it is extremely important that surgeons are able to weigh up the risks and benefits of any operation for (and with) individual patients. Sound judgment and decision making are key attributes of surgical expertise. This research aims to identify robust methods for assessing and teaching trainee surgeons in terms of their judgment and decision-making skills. This topic has received little previous research attention.

To start off the research programme, we conducted interviews about decisions in patient care. We then evaluated the usefulness of virtual reality simulation for training surgeons' operative decision making – similar to using flight simulators to train pilots. We then used a statistical method called 'judgment analysis' to measure how good surgical trainees are at estimating specific operative risks, based on hypothetical patient scenarios for differing surgical patients. This method was used to provide a basis for giving detailed feedback, to help trainees improve the accuracy of their judgments.

Finally, a half-day introductory teaching session entitled 'Judgment and decision making for surgical trainees' was developed and piloted at the Royal College of Surgeons. Additional pilot sessions are planned and if successful the programme will be expanded to form part of the formal postgraduate curriculum for surgical trainees.

In the long term, I hope this research will benefit all patients undergoing surgery. We now have a robust method for assessing how good surgeons are at estimating operative risks. It is hoped that the training innovations under way will not only help trainee surgeons to improve their own decision-making skills, but also to empower their patients to participate more fully in making decisions about their own care.

Fellowship/Sponsor
Rosetrees Foundation and Grand Lodge 250th Anniversary Fund

Miss Ros Jacklin

Site of study
Imperial College London,
St Mary's Hospital Campus

Supervisors
Professor Charles Vincent
Lord Darzi

Publications

American Journal of Surgery (in press)

American Journal of Surgery (in press)

Presentations

Association for Surgical Education, Washington, April 2007

Association of Surgeons of Great Britain and Ireland, Manchester, April 2007

'A good surgeon knows how to operate; a better one knows when to operate; and an excellent one knows when not to operate.'

Giving feedback on operative judgments.

identifying differences
between exstrophy and normal bladders

Fellowship/Sponsor
One year RCS Research Fellowship

Mr Navroop Johal

Site of study
Institute of Urology/
Institute of Child Health

Further funding
The Children's Research Fund, Liverpool (one year)

Supervisors
Professor CH Fry

Presentations

The Physiological Society, London, July 2006

The American Academy of Pediatrics, Atlanta, October 2006

Navroop at work.

The contractile properties of the human paediatric exstrophic bladder

Bladder exstrophy is a malformation of the bladder, in which the bladder and related structures are turned inside out. This occurs in 1 in 25,000 live births. Despite surgical closure at birth many patients remain with serious clinical problems that would affect them for the rest of their lives without correction – including severe incontinence, infections and kidney problems. We proposed that the source of the problems patients with bladder exstrophy suffer resides in abnormal contractile function of the muscle of the exstrophy bladder; there is no previous work to test this hypothesis.

Bladder specimens were collected from Great Ormond Street Hospital for children during surgery from children with bladder exstrophy and normal bladder. Tissue strips were placed in an organ bath. The contractile function was measured and compared between the two groups. Additionally the elasticity and the single cell responses of the bladder specimens were measured and compared between the two groups. Finally the structural properties were examined through microscopic assessments.

We have found some very interesting results and statistically significant differences between the exstrophy and normal bladder. The bladder is hypocontractile ie has reduced capability to contract. In addition the newborn exstrophy bladder is even more hypocontractile; but it has the ability to become more contractile once the bladder is closed. Interestingly the tissue is less elastic, suggesting changes in the structure of the bladder. However the single bladder cells were examined under a microscope, these worked 'normally'. So this suggests that the problems experienced by these children are due to the tissue structure of the bladder. This was confirmed through the histological experiments that show there is a reduced amount of muscle present. Additionally the newborn exstrophy bladder has a much less contractile ability than the older exstrophy bladder; this shows that early surgical correction enhances the chances of contractility.

'Bladder exstrophy has an incidence of 1 in 25,000. Children and adults with the condition need major reconstructive surgery to correct bladder function.'

investigating
structures of cancerous cells

The role of desmosomal cadherins in colorectal tumourigenesis

Desmosomal cadherins are a group of proteins that link adjacent cells together. The aim of this study was to determine the role of desmosomal cadherins in colorectal (bowel) cancer.

Although changes in desmosomal cadherin expression have been shown in other cancers, we have now demonstrated these changes in colorectal cancer. A variety of techniques were used to evaluate this. In healthy bowel only two types of desmosomal cadherin usually seen, desmocollin 2 (Dsc2) and desmoglein 2 (Dsg2). This study has demonstrated these are reduced colorectal cancer. In addition to this other desmosomal cadherins, not normally identified in the bowel, desmocollin 1 and desmocollin 3, were also found.

Little is known about the regulation of desmosomal cadherin gene expression. Therefore, the next part of our study looked at the mechanisms by which altered expression of desmosomal cadherins take place. Through studying factors known to be important in colorectal cancer, we were able to identify members of the CCAAT/enhancer binding protein (C/EBP) family of transcription factors regulate Dsc2 and Dsg2 expression in a colorectal cell line.

This work has demonstrated for the first time that desmosomal cadherin expression is altered in colorectal cancer. It has also shown a potential mechanism by which this occurs. Future work on this project will confirm these findings and include investigation of Dsc2 and Dsg2 expression in disease progression. Information from molecular markers may allow greater accuracy in the staging colorectal cancer in the future, allowing treatment to be directed accordingly.

Fellowship/Sponsor
One year RCS Fellowship

Miss Katherina Khan

Site of study
Epithelial Research Laboratory, University of Birmingham

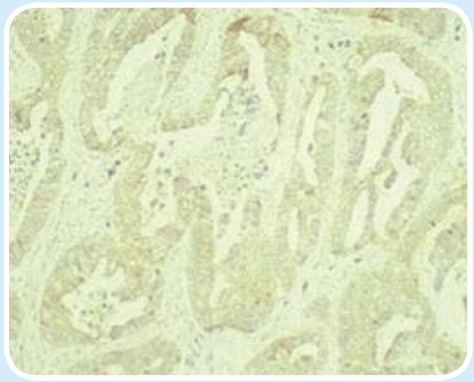
Supervisors
Mr Dion Morton

Publications

British Journal of Cancer (2006) 95, 1367_1370

'Each year, more than 35,000 people in the UK are diagnosed with bowel (colorectal) cancer. Bowel cancer is the second most common cause of death from cancer in the UK, and is responsible for 16,000 deaths each year.'

Dsc2 is localised at the cell membrane (brown staining) in normal colonic epithelium; (B) Dsc2 shows



Reduced Dsc2 staining is seen in colorectal cancer.

examining
how ET-1 stimulates fibroblast activities

Fellowship/Sponsor
One year joint RCS/Rosetrees Research Fellowship

Mr Jonathan Knowles

Site of study
University College London

Supervisors
Dr Marilena Loizidou

Publications

Ann R Coll Surg Engl 2006; **88**(1):69

Colorectal Disease 2006; **8**(Suppl. 2):30

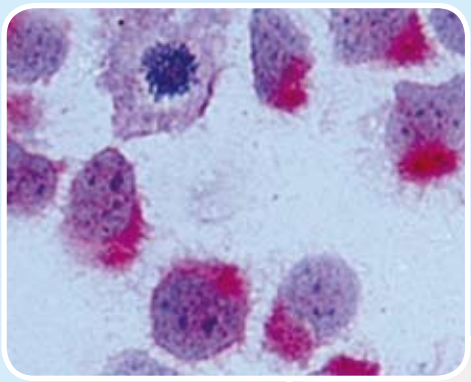
Presentations

Ninth international conference of endothelin (ET-9), Utah

The Annual Colorectal Surgery Conference, ACGBI (SAGE), Gateshead

Prizes

Tissue Sciences Laboratory Prize for Short Papers, ACGBI, Gateshead, July 2006



Fibroblasts stained for ET-1 using immunohistochemistry.

Endothelin-1 stimulates colorectal cancer adjacent fibroblasts

We examined how colorectal cancer can stimulate other cells to help cancers to develop. A hormone called ET-1, which is produced by colorectal cancers was used. This hormone was given to fibroblasts from the human colon and the responses measured. Fibroblasts are the body's construction cells; they produce and break down the collagens and support proteins that the body's cells live in. If cancer cells are unable to stimulate fibroblasts they will not develop into malignant tumours. We wanted to show that ET-1 was one of the hormones that could stimulate fibroblast activities.

Human fibroblasts were extracted from human colorectal cancer specimens. Fibroblast strains (n=6) were grown in laboratory conditions. The cells were exposed to ET-1. The changes in number of cells, how far they moved and their ability to contract was measured. Then blockers of ET-1 were used to show which of the two receptors for ET-1 were responsible for the effects. The expression of enzymes was measured using Western blot electrophoresis.

ET-1 stimulates proliferation, migration and contraction of fibroblasts (p<0.01). Proliferation was stimulated by ETA receptors (p<0.001), migration was stimulated predominantly by ETB receptors; contraction was stimulated by ETA and ETB receptors. ET-1 stimulated production of two out of three enzymes via both receptors.

Does the research build up on other investigations? It builds on previous work looking at the response of colorectal cancer cells to ET-1 and previous work extracting fibroblasts from colonic specimens. *How much research has there been into this area?* This is the only research to examine the responses of human colonic fibroblasts to this hormone. *Is it a long-term project that others will continue to develop?* It could be it provides interesting results about ET-1 and cancer and fibroblast interactions. Unfortunately there is no-one in the lab to take it on at the moment. *What is life like for patients with this condition?* Survival at 5 years remains around 50%. *How will it improve their quality of life?* The exciting thing about the drugs which block ET-1 is they are tablets with relatively mild side effects (unheard of for what is chemotherapy).

Jonathan and Dr Loizidou in the UCL tissue culture lab.

'Colorectal cancer associated fibroblasts respond to ET-1 via ETA and B receptors. Proliferating, migrating, contracting and producing matrix remodelling enzymes.'

developing
neurosphere transplantation for bowel function

Stem cell transplantation for Hirschsprung's disease

In children with Hirschsprung's disease some of the nerve cells that control the bowel are missing. This lack of nerve cells means that the bowel cannot function properly and without surgery to remove the affected part of the bowel the child will usually die. The results of surgery are still disappointing: 75% of children with Hirschsprung's disease suffer from incontinence even after surgery, 25% have bowel inflammation and 10% will go on to need a colostomy. This is because it is not possible to remove all the affected bowel without damaging the anal sphincter that allows us to control our bowel motions.

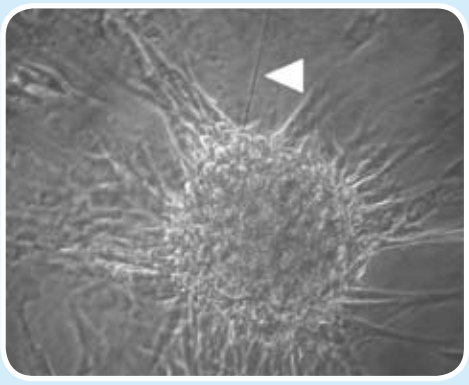
Our aim is to develop a technique that will allow replacement nerve cells to be transplanted into children with Hirschsprung's disease.

We take a small piece of bowel from children having surgery and break it down in the laboratory to individual cells. We can then grow nervous system stem cells from the bowel. These stem cells can produce more stem cells, nerve cells and nervous system support cells, and form floating clusters of cells called neurospheres. We have taken these neurospheres and transplanted them into pieces of bowel that lack a nervous system and are grown in the laboratory. After neurosphere transplantation we have measured the movement of the bowel and compared it to bowel that has not been transplanted.

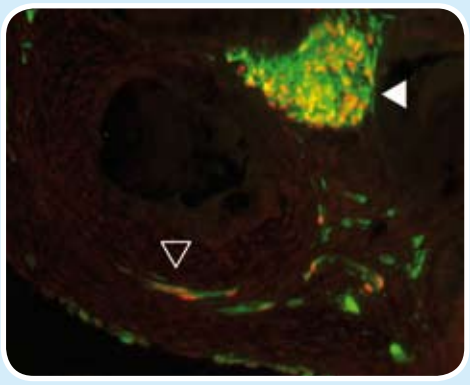
Our results show that neurospheres from human bowel are capable of forming a new nervous system. Furthermore, the neurospheres restore the rate of bowel contraction to that of a normal bowel.

The next stage of this research will be to transplant neurospheres into animals with Hirschsprung's disease. We hope that the lives of children with Hirschsprung's disease will be improved by reducing bowel inflammation, constipation and incontinence that can make their lives misery. Eventually, techniques like this may remove the need for surgery altogether.

'One child with Hirschsprung's disease is born every 72 hours in the UK.'



A human neurosphere. A nerve fibre (arrowhead) can be seen growing from the neurosphere.



A human neurosphere (solid arrowhead) transplanted into embryonic bowel that has no nervous system of its own. Nerve cells are shown in green and neurosphere cells are red. Nerve cells from the neurosphere have migrated into the bowel wall to form a new nervous system (hollow arrowhead).

Fellowship/Sponsor

Frances and Augustus Newman Foundation

Mr Richard Mark Lindley

Site of study

University of Liverpool and Institute of Child Health, Royal Liverpool Children's NHS Trust

Further funding

CORE (Digestive Disorders Foundation) (one year), a joint RCS/CORE funded award

Supervisors

Mr SE Kenny
Professor DH Edgar

Publications

Gut. 2007; **56**(4):489–96

Journal of Stem Cells. 2007; 2(2)

Presentations

New York Academy of Medicine, March 2006

19th International Symposium of Paediatric Surgical Research, Florence, October 2006

understanding genes
linked to arthritis

Fellowship/Sponsor
Henry Smith Foundation Research Fellowship

Mr Timothy Matthews

Site of study
Nuffield Department of Orthopaedic Surgery, University of Oxford

Further funding
Girdlestone Memorial Scholarship in Orthopaedic Surgery, University of Oxford (one year)

Supervisors
Professor Andrew Carr

Publications

J Bone Joint Surg Br 2005; **87-B**: 164

J Bone Joint Surg Br; **88**(4): 489–95, 2006

Presentations

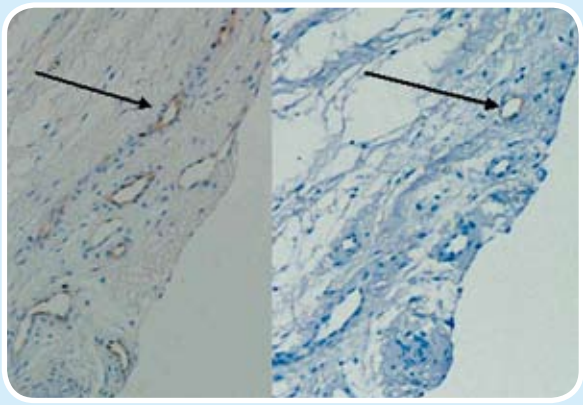
The British Elbow and Shoulder Society, 15th annual scientific meeting, Newport, June 2005

19th Congress of the European Society for Surgery of the Shoulder and Elbow (ESSSE), Rome, September 2005

Prizes

Kessel Prize for best paper, British Elbow and Shoulder Society, both 15th and 16th Annual scientific meetings, 2004 and 2005

Shoulder injury.



Torn tendon tissue showing stained blood and lymphatic vessels, the latter of which had not previously been reported in any tendon tissue.

Cellular responses in rotator cuff tears

Shoulder pain is a common yet debilitating problem; with the majority of those affected having 'wear and tear' changes to their rotator cuff. This specialised structure, which is a group of tendons fused together, serves to keep the shoulder in position during the movements of inward, outward and upward rotation. Severe degeneration of this structure leads to large tears, which often need to be repaired to alleviate the resultant pain, weakness and loss of function. It is not clearly understood what causes these tears and how they should best be treated.

Our aim was to investigate the quality of torn tendon tissue, in patients undergoing surgery, by analysing it under the microscope using contemporary techniques and placing needle electrode probes into the tissue. These probes enabled an assessment of how the tissue functioned. We then investigated, some months later, to see if any features from that previously analysed tissue quality could be identified as playing a role in the outcome of the surgical repair.

We found that as the tear size increased the healing potential of the tissue reduced significantly, both in terms of the cell types that were present and the reduced ability of the tissue to use oxygen efficiently. Repair was found to be more successful from torn tissue which showed good healing potential at the time of surgery.

These findings have not only advanced our understanding of the basic concepts of this disease process, but have also helped to identify which patients will benefit most from surgery and which surgical techniques may have advantages.

Further work is currently underway addressing many new questions that have now arisen in the light of this study.

'Shoulder pain is the second commonest limb problem that will require a person to consult their GP, and rotator cuff disease makes up the bulk of this.'

understanding
the process of synovial invasion

The role of membrane type-1 matrix metalloproteinase (MT1-MMP) in rheumatoid arthritis

Approximately 400,000 people in the UK have rheumatoid arthritis (RA), which can cause difficulty performing everyday activities such as dressing and eating. One cause of the difficulty occurs when the tissue lining the joints and surrounding tendons, termed synovium, becomes inflamed and 'invades' adjacent structures, resulting in joint deformity and tendon rupture.

Previous research has shown that this 'invasive synovium' differs from normal, non-invasive synovium in that the former produces greater amounts of destructive enzymes. However, the reasons why synovium invades in the first instance are not fully understood.

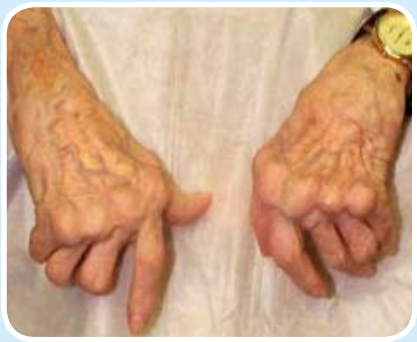
We suggested that one enzyme found in RA synovium, membrane type-1 matrix metalloproteinase (MT1-MMP), is critical for synovial invasion to occur. We tested this hypothesis by performing experiments that artificially induced loss and gain of MT1-MMP activity in RA cells.

Two methods evaluated synovial invasion. First, we examined cells invading out of specimens of RA synovium, and we identified the trends between treatment groups.

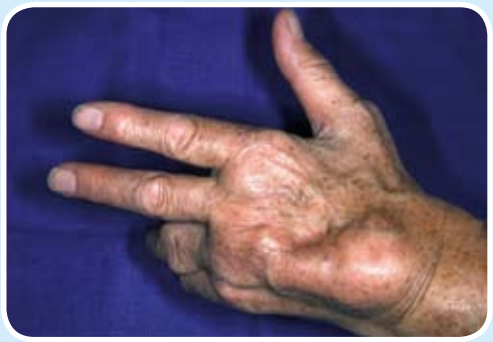
Secondly, we established a novel method of measuring invasion, using cells extracted from pieces of tissue donated by rheumatoid patients. The sole use of these cells (without the rest of the tissue) enabled us to make a precise comparison of how many cells invaded after loss and gain of MT1-MMP activity.

From these we discovered that invasion is dependent upon MT1-MMP. Inhibition of MT1-MMP halted synovial invasion and its over-production promoted invasion. This suggests MT1-MMP is a key molecule in the process of invasion.

Our findings indicate that the process of synovial cell invasion is dependent upon MT1-MMP and we now have an enhanced understanding of the process of invasion. This work has therefore identified a potential target to be blocked that could lead to the development of new drug therapies in rheumatoid arthritis.



Joint Deformity in Rheumatoid Arthritis can limit the ability to perform everyday activities.



Tendon rupture in Rheumatoid Arthritis. Rheumatoid Arthritis of the hands affects the tendons as well as joints. In this case breakage of the tendons has occurred so this man is unable to lift up his ring and little fingers.

Fellowship/Sponsor
Enid Linder Foundation Surgical Research Fellowship

Mrs Mary-Clare Miller

Site of study
Kennedy Institute of Rheumatology Division, Imperial College London

Further funding
Kennedy Institute of Rheumatology, ARC Core Grant (two years)

Supervisors
Professor Jagdeep Nanchahal
Dr Yoshifumi Itoh

Presentations

International Federation of Societies for Surgery of the Hand Congress, Sydney, March 2007

British Society for Surgery of the Hand Autumn Meeting, London, November 2006

Prizes

Journal of Hand Surgery Prize for Best Paper, British Society for Surgery of the Hand Autumn Meeting, November 2006

Best Paper Award, Australian Hand Surgery Society Meeting, March 2006

'Approximately 400,000 people in the UK have rheumatoid arthritis, and in over 80% of them, their hands are affected. This research could help those with rheumatoid arthritis of the hands.'

reducing neurocognitive problems following coronary artery surgery

Fellowship/Sponsor
RCS/Freemasons Research Fellowship

Mr Reza Motallebzadeh

Site of study
Department of Cardiac Surgery, St George's Hospital

Supervisors
Miss Marjan Jahangiri

Publications

Ann Thorac Surg 2007;83:475–82

Ann Thorac Surg 2006;82:615–9

Presentations

86th annual meeting of The American Association of Thoracic Surgeons, Pennsylvania, May 2006

British Society of Cardiology, Glasgow, April 2006

Prizes

John Parker Medal for best presentation at Society of Cardiothoracic Surgeons of Great Britain and Ireland Meeting, 2004

Finalist for European Association of Cardio-Thoracic Surgery Young Cardiac Investigator's Award, 2004

'Neurocognitive complications following coronary artery bypass surgery (CABG) can occur in up to 80% of patients. A surgical approach in which a heart lung machine is not used (off-pump or 'beating-heart' surgery) may reduce these complications, perhaps because it results in fewer emboli (air bubbles or blood clots) passing into the brain.'

Neurocognitive function, cerebral emboli, and S100b after on-pump and off-pump coronary artery bypass surgery: a randomised study

A study of 212 patients undergoing either on-pump CABG (conventional non-beating heart surgery) or off-pump CABG was carried out. The aim of the study was to determine if there are fewer cerebral emboli during off-pump CABG and whether this results in better neurocognitive function compared to on-pump surgery.

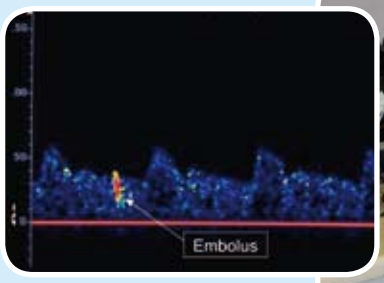
Neuropsychological function was analysed before surgery and post-operatively on the day of discharge from hospital, at 6 weeks and at 6 months follow-up. The neuropsychological examination tested the patient's memory, motor skills, reaction time and attention.

Transcranial Doppler ultrasound was carried out on both middle cerebral arteries simultaneously throughout each operation. This is a non-invasive technique of measuring blood flow to the brain. The signals were recorded onto digital tape, and the total number of embolic signals was counted.

The average number of emboli during on-pump CABG was 1,600, but it was just 9 during off-pump surgery. Patients who underwent off-pump CABG had better neurocognitive function compared to on-pump patients at discharge from hospital. However, at six weeks and by six months, there was no difference between the two groups.

This is the only large and randomised study to date that has compared both cerebral emboli and neurocognitive function between on-pump and off-pump CABG. There is little difference in brain function at 6 weeks and 6 months between patients undergoing on-pump or off-pump CABG, and the number of emboli during surgery only influences brain function in the immediate post-operative period. The cause of cerebral injury after CABG is multifactorial, with emboli as one factor in a myriad of other processes that can influence brain function.

The follow-up of these patients will now be extended to three years from the date of surgery.



Appearance of an embolus ('blood clot') on TCD ultrasound recording.


Reza reading data from transcranial Doppler ultrasound recording.

determining the role
of 'foreign' cadherins in colorectal cancer

Christopher with a patient.

Fellowship/Sponsor
Sir Alan Parks Research Fellowship

Dr Christopher Neal

Site of study
Leicester General Hospital/
University of Leicester

Supervisors
Mr David P Berry

Publications
Eur J Cancer 2006; **42**(12): 1728–1743

Surgery 2006; **24**(4): 120–125

Presentations
7th Congress of the European Chapter of the International Hepato-Pancreato-Biliary Association (EHPBA), Verona, June 2007

7th World Congress of the International Hepato-Pancreato-Biliary Association (IHPBA), Edinburgh, September 2006

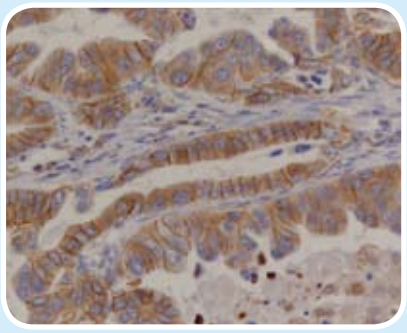
Dysregulation of the classical cadherin repertoire in colorectal cancer

Colorectal cancer (CRC) is the second commonest UK cancer, causing around 10 per cent of all cancer-related death. Most of these deaths result from cancer spread to distant sites, particularly the liver. Healthy tissue structure is dependent upon proteins (cadherins) that are expressed on the cell surface and act to 'glue' adjacent cells together. Loss of normal cadherins leads to break down of tissue structure and is associated with cancer development and spread. Studies in several cancer types have recently shown that gain of 'foreign' cadherins, which are not normally expressed in a particular healthly tissue, may also be important to cancer development. This project aimed to determine the role of 'foreign' cadherins in CRC.

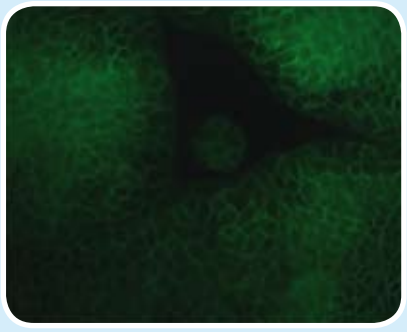
Involvement of 'foreign' cadherins in CRC was demonstrated by their detection in 150 resected primary CRC, as well as in secondary deposits resulting from cancer spread to other organs. Remarkably, 'foreign' cadherins were detected in over 90% of CRC, with expression maintained in secondary deposits. Importantly, expression of 'foreign' cadherins also correlated with tumour progression. In order to determine the means by which 'foreign' cadherins affect cancer cell behaviour, cadherin expression was then manipulated in cancer cells *in vitro* and effects on cellular behaviour observed. These experiments revealed that foreign cadherins affect cancer cell behaviour through stimulating cellular division, slowing cell death and encouraging invasion.

The results of this project indicate that 'foreign' cadherins may be used to predict the degree of disease spread in patients with CRC and, particularly given their continued expression in secondary deposits, may also represent novel drug targets. Several novel chemotherapy agents targeting cadherins are currently in development. The data yielded by this study suggest that the targeting of cadherin-expressing tumours with these agents may yield significant benefit to patients with CRC in the future.

'Colorectal cancer (CRC) is the second most common malignancy in the United Kingdom, accounting for around 10 per cent of all cancer deaths.'



Detection of Cadherin-3 in resected primary colorectal cancer using immunohistochemistry.



Detection of Cadherin-3 in the HCT-116 colorectal cancer cell line in vitro using immunofluorescence.

genetic abnormalities
causing crystal formation in joints

Fellowship/Sponsor
Joint Royal College of Surgeons and Botnar Surgical Research Fellowship

Mr Chris Peach

Site of study
Nuffield Department of Orthopaedic Surgery, University of Oxford

Supervisors
Professor Andrew J Carr

Publications

Clin Orthop Relat Res 2007; **462**:67–72

Trends Mol Med. 2005 Apr; **11**(4):186–91

Presentations

20th congress of the European Society for Surgery of the Shoulder and the Elbow, Athens

The British Elbow and Shoulder Society 17th annual scientific meeting, Edinburgh

Prizes

Stefan Galeski Travelling Fellowship, Royal College of Surgeons of England

An investigation into the role of genetics and crystals in the development of cuff tear arthropathy

Cuff tear arthropathy is a chronic disabling arthritis affecting the shoulder. The cause of the disease is poorly understood and the limited options available for treatment are far from satisfactory. It is known that the majority of patients have a deposition of calcium crystals in the shoulder joint, although debate surrounds whether their presence triggers the arthritis or whether they are a by-product of the disease.

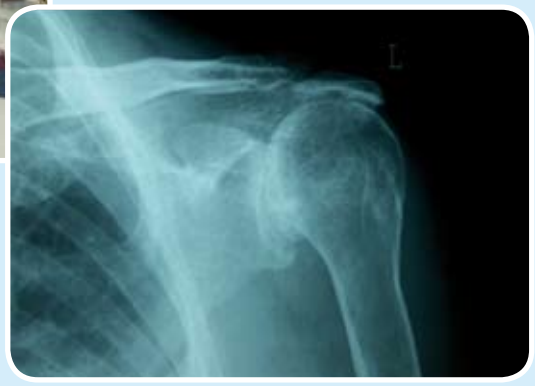
We aimed to investigate whether these patients had genetic variants in genes known to control pathways that can lead to pathological crystal formation. In addition, we wanted to investigate the affect of any genetic abnormalities on the function of human cartilage cells.

We found that patients with cuff tear arthropathy had genetic abnormalities in genes controlling calcium crystal deposition. We also demonstrated that when these genetic variants occur in cartilage cells, they have a direct affect on the function of the protein they encode. This provides strong evidence that crystal formation in joints, which is under genetic control, is a major factor in disease development and progression.

The findings of the investigation increase our knowledge of the pathology of the condition. Although this will not directly alter the current surgical treatments for the disease, it offers the possibility that the biological pathways responsible are modifiable by drug treatment. Further investigation is needed to examine how these functional changes, brought about by the genetic abnormalities, can be harnessed in vivo.

'Patients with cuff tear arthropathy have variants in genes that predispose them to calcium crystal formation.'

Chris sequencing genes in the Botnar Research Centre in Oxford.



X-ray showing severe shoulder arthritis typical of patients with cuff tear arthropathy.

advancing
the treatment of bladder cancer

Thiothymidine combined with UVA and raltitrexed as a potential novel therapy for bladder cancer

Bladder cancers that are treated by surgical resection often recur and may require chemical treatments administered into the bladder to reduce disease progression. Thiothymidine is a molecule that closely resembles thymidine – an essential building block of DNA. Cells can utilise thiothymidine in place of thymidine for growth, however, when these cells which have been pretreated with thiothymidine are then exposed to ultraviolet A light (UVA) the thiothymidine molecule undergoes a rapid photochemical reaction causing lethal DNA damage.

The aims of this project are to investigate whether thiothymidine can be used in combination with UVA and another drug called raltitrexed (which may increase the sensitivity to UVA) as a novel treatment for bladder cancer.

Using bladder cancer cells grown in the laboratory we have shown that thiothymidne sensitises bladder cancer cells to low doses of UVA. Furthermore, the addition of raltitrexed increases the incorporation of thiothymidine into cellular DNA and thus augments the potency of this treatment.

Our work has shown that when thiothymidine is combined with UVA, the mechanism of DNA damage is through the formation of DNA – DNA crosslinks as well as DNA-protein crosslinks, which are likely to interrupt the machinery required for cell division and growth. This treatment initiates a type of cell death called apoptosis (a form of cellular suicide).

We have developed an animal model for bladder cancer and are currently investigating the uptake of thiothymidine into tumours when administered into the bladders or injected into the blood. Using a fine optic fibre that can deliver UVA light into bladders we plan to test this treatment.

We have collected fresh bladder tumour samples from patients undergoing bladder cancer operations to show that human tumours can also absorb thiothymidine.

We are optimistic that his novel therapy could potentially benefit the many patients with bladder cancer and may be useful in the treatment of other diseases too.

Measuring thiothymidine incorporation into DNA using liquid chromatography mass spectrometry.

Fellowship/Sponsor
One year RCS Research Fellowship

Mr Simon Pridgeon

Site of study
Northern Institute for Cancer Research

Further funding
British Urological Foundation
(six months)

Supervisors
Professor Alan V Boddy

Presentations

The American Association for cancer research annual meeting, Los Angeles 2007

The European Association of Urology annual meeting, Paris 2006

'Bladder cancer is the fifth commonly diagnosed malignancy in the UK.'

Simon with supervisor Professor Alan Boddy examining histological sections of bladder tumours.

restoring VEGF
to melanoma cells to reduce tumour growth

Fellowship/Sponsor
Joint BAPS/RCS Fellowship

Mr Rowan Pritchard Jones

Site of study
Microvascular Research Laboratories, University of Bristol

Supervisors
Mr J Kenealy
Dr D Bates
Dr S Harper

Publications

Melanoma Research. 16 Supplement **1**: S8–9, September 2006

Cancer Research 2004 Nov 1; **64**(21):7,822–35

Presentations

European Society of Plastic Reconstructive and Aesthetic Surgery (ESPRAS) appointed meeting, Portugal, 2006

Melanoma X, Amsterdam, 2006

Prizes

Hunterian Professorship, Royal College of Surgeons of England, 2006

Terence Ryan Award, British Microcirculaion Society, 2004

Expression of a novel inhibitory form of VEGF in skin and skin cancer

Anti-angiogenic therapy (the inhibition of blood vessel development and growth) is now the fourth treatment modality for cancer alongside surgery, radiotherapy and chemotherapy. Malignant melanoma responds well only to surgery, and the successful prediction of potential metastatic spread based on the characteristics of the primary tumour (ie tumour thickness) remains elusive in 15% of patients who will go on to suffer spread of a seemingly low grade melanoma.

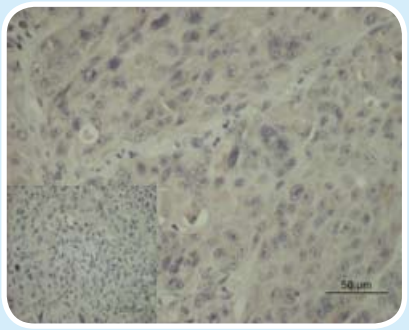
The newly discovered anti-angiogenic molecule, VEGF165b, was explored for prognostic and therapeutic potential in melanoma.

'Angiogenesis, the growth of blood vessels, is an absolute prerequisite for cancer growth and spread. Without it, tumours can grow no more than 1–2mm in size.'

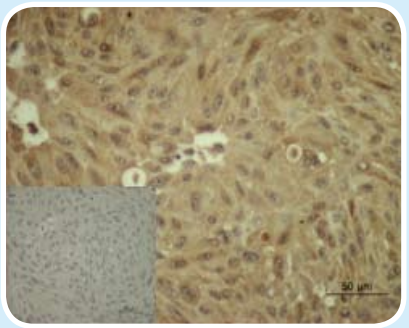
The first stage of the project looked at the expression of VEGF165b in primary melanoma and found a strong correlation to outcome. If a melanoma successfully 'switches off' this protective molecule, it is able to acquire a blood supply and potentially spread around the body. Identifying an early melanoma that had succeeded in this respect better predicted later spread than tumour thickness alone would suggest. The challenge was to develop a potential treatment for such high-risk patients.

This was explored by restoring the protective VEGF165b to melanoma cells in the laboratory, and measuring the subsequent growth of the tumour in a living model of melanoma metastasis. This study showed a significant reduction in tumour growth rate and size, indicating enormous therapeutic potential for this endogenous molecule.

This project has offered not only a potential therapy to melanoma patients, but has also demonstrated a principal of cancer inhibition that now appears to hold true for colorectal, breast, prostate and renal cell cancer as well. The other potential benefit of this molecule is that it is naturally occurring in the body and not a toxic new chemical. Work continues to bring this novel treatment to the clinical setting.



A primary melanoma that later metastasized showing no brown staining indicative of the protective $VEGF_{165}b$ protein.



A primary melanoma that has never metastasized showing high levels of $VEGF_{165}b$ protein expression characterized by the intense brown staining.

researching
the conditions leading to struvite stone formation

The physico-chemical basis of magnesium ammonium phosphate (struvite) stone formation

Magnesium ammonium phosphate (struvite) stones account for 10–15% of all urinary tract stones and can fill the whole renal pelvis – forming 'staghorn calculi'. They commonly occur in patients with urinary tract infections. These stones are particularly problematic because they grow rapidly, generate considerable pain, and are difficult to remove completely with surgery, further creating problems of recurrence. Untreated staghorn stones can lead to sepsis and renal failure.

Current medical therapies (eg dietary manipulation, urine acidifying agents) have had limited success and surgical removal of the stone is the mainstay of treatment. This project aims to understand the conditions that lead to the crystallisation of struvite stones so that strategies can be developed to prevent their occurrence. At present, very little is known about the physico-chemical conditions that result in struvite stone formation. This lack of understanding has two explanations: i) the particular ionised concentrations of the constituents (eg Mg^{2+}, NH_4^+, and phosphate) in the urine are unknown; ii) the prevailing urinary chemical conditions that would modulate struvite crystal formation are also unclear (eg pH, osmolality, other urinary constituents).

We have manufactured and developed Mg^{2+}- and NH_4^+-selective electrodes, which have allowed us to make the first measurements of these constituents in undiluted human urine. We have successfully validated the NH_4^+-selective electrode against a standardised method used at the Institute of Hepatology in UCL. The novel advantages of these ion-selective electrodes are evident by their robustness, and their ability to provide rapid and reproducible readings in undiluted human urine samples.

We are currently measuring NH_4^+ and Mg^{2+} in urine samples from patients with and without struvite stones. The aim is to compare the urine compositions from both groups and eventually attempt to manipulate the conditions in order to reduce the rate and extent of $MgNH_4PO_4$ (struvite) crystal growth in urine. Further research will identify useful agents and regimes that may be used therapeutically.

Professor Chris Fry explaining the finer aspects of ion-selective electrodes.

Fellowship/Sponsor
Surgical Research Fellowship – Rosetrees foundation

Mr Senthy Sellaturay

Site of study
Institute of Urology, University College London

Supervisors
Professor Chris Fry

Publications
BJU International. 2007 June; **99**(4): 46

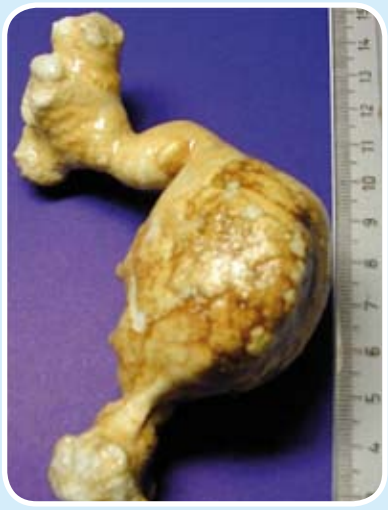
24th World Congress Endourology. 2006 August; p105

Presentations
World Congress of Endourology, Ohio, August 2006

BAUS, Glasgow, June 2007

'Kidney (renal) stones commonly affect approximately 10–15% of the population at some point in their lives. Staghorn stones can lead to sepsis and renal failure in certain instances.'

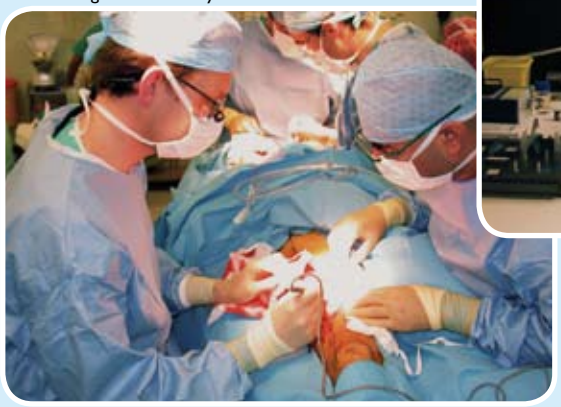
Renal Staghorn Stone.



devising more effective techniques to combat pancreatic cancer

Fellowship/Sponsor
Freemasons Research Fellowship

Carrying out laboratory assays: methylation analysis using the pyrosequencers.



Head and neck surgery: two site operating with resection of a tumour and preparation of tissue for immediate reconstruction from the thigh for free tissue transfer occurring simultaneously.

Mr Richard Shaw

Site of study
University of Liverpool and University Hospital Aintree

Further funding
Cancer Research UK, British Association of Oral and Maxillofacial Surgeons, Department of Health (one year)

Supervisors
Dr Janet Risk

Publications
Nucleic Acids Res 2006; **34**(11):e78.

Br J Cancer 2006; **94**(4):561–8

Presentations
University of Michican, Surgical Grand Rounds, Michigan, September 2006

International Congress in Oral Cancer, Grado, April 2006

Prizes
Paul Toller Prize 2006 of the British Association of Oral and Maxillofacial Surgery for basic science surgical research

Prize for Best Research Presentation, Royal Liverpool University Hospital Research & Development open day, October 2005

'The incidence of head and neck cancer is over 500,000 per annum worldwide and tumours of the oral cavity are the commonest type in the UK today.'

Epigenetic biomarkers in head and neck cancer

While surgical treatment for head and neck cancer is relatively successful, methods of diagnosis and staging are still crude. Adjuvant treatment has permanent effects on quality of life such as speech and swallowing so needs to be used only when needed. This biomarker research is focused on the desire to design tests that can accurately detect minute amounts of cancer tissue, termed 'minimal residual disease' which might progress to untreatable recurrence if not diagnosed and treated early.

This work starts with the collection of specimens kindly donated by a series of cancer patients. 1,300 separate specimens were collected from a cohort of 110 patients in this study. It is important to define a panel of genes in which abnormalities were specific to cancer and ultimately would be reliable to depend on in clinical trials. We were particularly interested in an area called epigenetics where genes can seem undamaged but are switched off by methylation in the promoter regions. In a typical tumour, around 10–12 genes might have direct damage (eg mutation) but around 100–150 genes are abnormally silenced by methylation. This also opened up the problem of just how accurate existing molecular assays for DNA methylation were. We worked on a new technique called pyrosequencing and have pioneered new assays for DNA damage in Liverpool. These techniques were applied to clinical specimens for the first time during this fellowship and these results have now been published.

Having clarified some of the more basic science and technical issues, it was important to perform many assays on the clinical specimens. In particular, the work on surgical margins and surrogates seemed to show the most promise and these two areas have generated new research projects and successful grant applications. This work has reinforced the necessity of multidisciplinary working, with surgery, oncology, pathology working alongside molecular biology to drive the field forwards. Several undergraduate, postgraduate and clinical projects have grown from this work as well as a new clinical senior lecturer position in the School of Cancer Studies in the University of Liverpool.

analysing gene
ratios for use in prostate cancer diagnosis

The tumour–stroma distribution of degradome components in human prostate cancer

Our aim was to identify whether specific molecules from a family of genes (proteases) are useful markers and possible targets for treatment in men with prostate cancer. We had previously reported on some genes that were altered in prostate tissues, but had used whole tissues that contain a mixture of benign and cancerous tissues. This was not felt to be representative as the mixture of cells is likely to cloud the true expression of these molecules

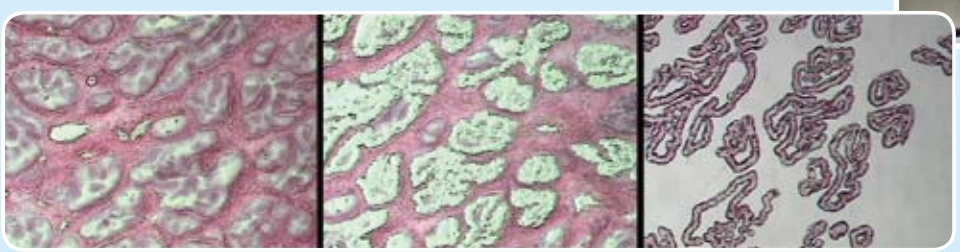
We used a technique called laser capture microdissection (LCM), a relatively new tool to separately analyse components of prostate tissues for the expression levels of these molecules. This technique allows the specific separation of cancerous cells from normal cells and thus gives us a better impression of the true levels of expression of these molecules. Having identified the genes that are greatly altered, we used a robust mathematical model to analyse gene ratios that can be used for diagnosis of prostate cancer.

We identified that the genes that are very significantly altered in expression in prostate cancer including Hepsin, MMP26, Maspin and TIMP4. Other genes that are altered, but not as significantly were MMP2 and uPAR. We identified that ratios involving the 4 most deranged genes were highly diagnostic of prostate cancer, the strongest relationship being that between MMP26 and TIMP4, which was also able to distinguish prostate cancer from benign and pre-cancerous lesions in almost all cases.

'A four gene ratio has been identified which is highly diagnostic of prostate cancer in tissues.'

The findings of this project have sparked major investigations within our and our sister groups and is hoped to advance our understanding of the process involved in the spread of prostate cancer.

It is important to be able to identify which patients will require treatment as this will reduce the patients being over-treated by surgery or radiotherapy. It is hoped that molecules may serve as more robust markers of disease aggressiveness when used in conjunction with traditional tools such as the PSA blood test, the prostate biopsy and scans.



Laser capture microdissection of a prostate tissue sample.

Fellowship/Sponsor
Lillian Coleman Fellowship

Mr Chitranjan Shukla

Site of study
University of East Anglia and Norfolk and Norwich University Hospital NHS Trust

Supervisors
Professor Dylan Edwards

Publications

Laser capture microdissection in prostate cancer research: establishment and validation of a powerful tool for the assessment of tumour–stroma interactions. Submitted and awaiting for reviewers comments

The tumour–stroma distribution of degradome components in human prostate cancer (in preparation)

Presentations

European Association of Urology annual meeting, Berlin, March 2007

British Association of Urological Surgeons meeting, Glasgow, June 2007

The Arcturus Pixcell IIE LCM system in the Edwards laboratory.

the role of mucin genes
in the development of laryngeal cancer

Fellowship/Sponsor
Frances and Augustus Newman Foundation

Mr Fabian Sipaul

Site of study
Mucin Research Laboratory,
Bristol Royal Infirmary

Supervisors
Dr Anthony Corfield
Mr Stephen Wood
Professor Martin Birchall

Publications

Molecular Immunology 2006, **43**(6): 725–30

Clinical Oncology 2004, 16(7) Supplement S20

Presentations

Otolaryngological Research Society (ORS) spring meeting, Newcastle, April 2004

5th European Congress of Oto-Rhino-Laryngology Head and Neck Surgery (EUFOS), Rodos, September 2004

'Squamous cell carcinoma of the voice-box is the most common head and neck cancer in the Western world and represents approximately 1 in 100 of all cancer types in men. If detected early enough, almost all patients with this type of cancer are curable without the need to surgically remove their voice-boxes.'

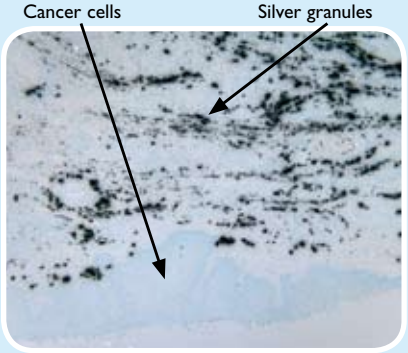
A study of mucin genes and trefoil peptides expression in normal and abnormal larynx

The aims of this study are to characterize the expression of mucin (MUC) and trefoil peptide (TFF) genes and their protein products in the normal human voice-box (larynx) and study the patterns of expression of these molecules in the larynx of smokers, in laryngeal pre-cancer and cancer. This study may help to identify a cancer marker among the mucin genes and trefoil peptides.

Biopsies are taken from normal controls (non-smokers without laryngeal signs or symptoms), and from smokers undergoing routine E.N.T. operations. The site of biopsy is the false cord of the upper part of the larynx. Archival tissue from patients with pre-cancer and cancer of the larynx is used to study mucin gene and trefoil peptide expression in these disease processes. Levels of mucin and trefoil peptide gene and protein products in the lining of the larynx are correlated with smoking habit and compared with those in the pre-cancerous state and laryngeal cancer. The archival specimens are further subdivided into those with and without previous radiotherapy.

The expressions of MUC4, MUC5AC and MUC6 appear to be altered in the cancer group as compared to the diseased groups. This suggests that some mucin genes may be involved in the development of laryngeal cancer. TFF3 mRNA is highly expressed in all groups and its level of expression appears to be altered in pathological states. It may have also have a role in the development of laryngeal cancer. Smoking only appears to affect the expression of some mucin genes and TFFs. Radiotherapy does appear to affect the expression of some mucin genes and all three TFFs. Future studies will have to take this into consideration.

Patients with early cancer of the larynx have a very good outcome with more than 90% chance of a cure with radiotherapy. Those who have recurrence following radiotherapy will still do well with surgery. Following removal of their larynges, patients have to adjust to the fact that they cannot speak normally, their swallowing process has changed and they are breathing through a hole in their neck. Early detection and close follow-up may allow patients to keep their larynges, be cured of cancer and maintain their quality of life.



Silver granules staining on a laryngeal cancer specimen denoting location of MUC5AC genes.


Dr A Corfield and Fabian scrutinising staining pattern on an autoradiograph.

solutions to prevent
joint replacement implants becoming loose

The role of matrix extracellular phosphoglycoprotein (MEPE) in bone formation and the development of nanoscaled biomaterials – its application to the bone implant interface

Over the last 100 years, total joint replacement for arthritis has been a true success story for modern medicine. The removal of pain and improvement in function for those patients with severe arthritis is astonishing. However, the down side is that over time the implants can become loose. This returns the patient to having a painful joint once more. The purpose of this project was to provide possible solutions on how to enhance an implant's ability to reduce this loosening process. This involves having a greater understanding of cell behaviour taking place between the bone and metal surface.

We looked at a novel bone protein called MEPE and a biomaterial called chitosan. This involved growing animal models either with the MEPE protein or on a chitosan surface, or a combination of both.

We have found that a modified version of this novel protein (MEPE) increased cell stickiness, activity and bone formation. This provides evidence that modified MEPE may be a protein candidate, which in the future will be incorporated onto a total joint replacement surface. To allow us to use proteins such as MEPE, a temporary scaffold is required to allow its gradual release into the surrounding bone. The example we worked on was chitosan. Our experiments showed us that this surface when modified could allow bone to successfully grow and develop.

Our work illustrates new areas of potential for both chitosan and MEPE. This area is still in its relative infancy regarding technology development, however its potential has now been realised. Our work is being continued by an orthopaedic research fellow, with sponsorship for another 3 years by the Arthritis Research Council.

Although the impact on patient's lives does seem distant in such a project, this biological approach will provide the future advances in orthopaedic surgery that will have a significant impact to people's lives. Nevertheless, it does require careful and methodical research like ours, to ensure patients safety.

Fellowship/Sponsor
Shears Northern Research Fellow

Mr Andrew Sprowson

Site of study
Newcastle University

Further funding
ARC, Arthritis Research Campaign, (one year)

Supervisors
Dr MA Birch

Publications
JBJS 2006;88-B:SUPP II

JBJS 2006;88-B:SUPP III

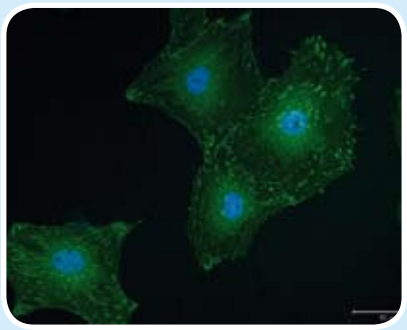
Presentations
European Orthopaedic Research Society, Lisbon, June 2005

British Orthopaedic Research Society, RNOH, Stanmore, July 2005

Prizes
Prize Session British Orthopaedic Research Society, Manchester, September 2004

'Over 80,000 major joint replacements are performed every year in the NHS. At 10 years over 10% of these will fail due to the implant becoming loose, without any sign of infection.'

Dr Mark Birch and Andrew viewing stained bone cells.



Bone cells stained to assess cell sticking to a surface.

avoiding
insulin injections for children

Fellowship/Sponsor
RCS Surgical Research Fellowship

Mr Warwick Teague

Site of study
Paediatric Surgical Research Laboratory,
Nuffield Department of Surgery,
University of Oxford

Supervisors
Mr Paul RV Johnson

Publications
Journal of Pediatric Surgery 2007; **42**(1):153–159

Journal of Pediatric Surgery 2006; **41**(2):347–351

Presentations
40th Annual Meeting of the Pacific Association of Paediatric Surgeons together with the Annual Scientific Meeting of the Australasian Association of Paediatric Surgeons, Queenstown, 2007

37th Annual Meeting of the American Pediatric Surgical Association, South Carolina, 2006

Prizes
Peter Paul Rickham Prize (Best Paper) British Association of Paediatric Surgeons, 51st Annual International Congress, Dublin, 2005

Novartis Prize (Best Paper) XVIIth International Symposium on Paediatric Surgical Research, Liverpool, 2003

Pancreatic islet mesenchyme-to-epithelial transition: a novel stem-cell source?

Pancreatic islet transplantation is a minimally invasive alternative to insulin injection for the treatment of type 1 diabetes mellitus (T1D), which has achieved insulin-independent rates >80% in recent clinical trials. A shortage of human donor islets limits the wider application of this potentially curative treatment. Stem cells may provide an alternative source of islets for transplantation. However, two key questions must be answered before T1D stem cell-based therapies can be realised. First, what stem cells are best suited to islet differentiation? Second, which strategy will optimally derive tissue for reversing T1D?

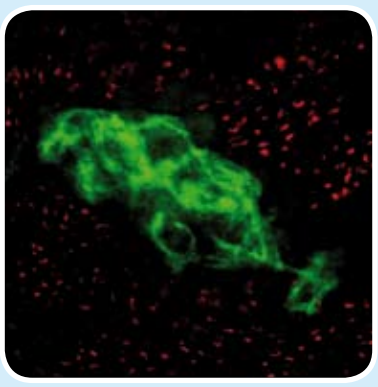
This project aimed to address these questions by investigating normal islet development. During development the pancreas comprises two fundamental tissue types: endodermal epithelium and surrounding foregut mesenchyme. Until recently there was no evidence to refute the dogma that islets are exclusively derived from pancreatic endodermal epithelium. Contrary to this, it was hypothesised that foregut mesenchyme is also able to undergo islet differentiation by mesenchyme-to-epithelial transition (MET), as is the case for organs such as the kidney.

Utilising an in vitro animal model, I mapped the fate of foregut mesenchyme cells during pancreatic islet development. This showed foregut mesenchyme can indeed give rise to both insulin-producing beta-cells and glucagon-producing alpha-cells. Therefore, foregut mesenchyme may be an unrecognised source of stem cells capable of islet differentiation. I then elucidated principal mechanisms responsible for islet MET. The signalling pathways instructing the transition from mesenchyme to islet cell are the subject of ongoing investigations within our laboratory.

Together, these and future studies may assist the design of differentiation strategies to coax mesenchymal stem cells into becoming islet cells suitable for transplantation. If successful, stem cell-based treatments will revolutionise the life of patients with T1D, including newly diagnosed children, who will be spared from daily insulin injections and life-threatening diabetes complications.

'Mesenchymal stem cells may provide a cure for patients of all ages with diabetes.'

Warwick performing a micro-dissection of embryonic tissue.



Example of a mesenchyme-derived islet surrounded by epithelial cells (nuclei shown in red with insulin staining shown in green).

developing
ways to kill tumour cells

Tim teaching an SHO how to do a hernia repair in theatre.

Fellowship/Sponsor
MRC/RCS Clinical Research Training Fellowship

Mr Tim Underwood

Site of study
Cancer Sciences Division, University of Southampton

Supervisors
Dr Jeremy Blaydes

Presentations

American Association for Cancer Research Annual Conference 2006, Washington DC, 2006

Society of Academic and Research Surgery Annual Meeting 2005, Newcastle, 2005

Prizes

Best Poster Presentation prize, Academy of Medical Sciences/Royal College of Physicians annual clinical scientist meeting, 2006

Inhibition of the PAX3 proto-oncogene by p53

Cancer is disease caused by the accumulation of genetic mistakes over time. When these genetic mistakes give the normal cell a growth advantage over its neighbours a tumour is formed. Elaborate cellular systems exist to detect and repair genetic mistakes (mutations) and help prevent cancer formation. One such example is the 'genetic policeman': p53. The p53 protein is responsible for sensing dangerous genetic mutations and forcing the affected cell either to undergo repair of its damaged DNA or commit suicide. Because of this vital function in cancer prevention p53 is itself mutated in over 50% of all human tumours. In the remainder of human cancers it is believed that the p53 operational pathway is in some way disrupted. An example of one such tumour type is malignant melanoma, a condition that is increasing quickly in the U.K. Early melanomas are treated successfully by surgery but late-stage melanoma has a very poor prognosis and is resistant to chemotherapy. During my PhD I have studied the activity of a protein (PAX3) that is normally only expressed in the embryo but has been found in over 70% of malignant melanoma specimens. Using a range of molecular biology techniques I have demonstrated that PAX3 directly inhibits p53 function by reducing both the amount of p53 present in the cell and its activity. Furthermore I have shown that PAX3 is a potential therapeutic target in malignant melanoma. These findings will be used to screen a library of molecules to identify a chemical capable of preventing PAX3 activity in melanoma and a potential novel agent for use in late stage melanoma.

'I have shown that PAX3 is a potential therapeutic target in malignant melanoma.'

evaluating the ratio
of stimulating and inhibiting forms of VEGF

Fellowship/Sponsor
Enid Linder Research Fellowship

Mr Alexander Varey

Site of study
University of Bristol

Supervisors
Dr David Bates

Publications

Microcirculation Sep 2006; **13**(6):511–34

Colorectal Disease 8 Jul 2006; (s2), 99–102

Presentations

American Association of Cancer Research Annual Meeting, Los Angeles

British Microcirculation Society Annual Meeting, Belfast

Prizes

Hunterian Professorship, Royal College of Surgeons of England

Young Investigator of the Year, British Oncological Association

'Only about 1 in 5 patients treated with Avastin gain significant benefit.'

Alex and supervisor, Professor David Bates inspecting successful inhibitory VEGF gene cloning.

The role of anti-angiogenic VEGF isoforms in cancer

As cancers grow in size, so they must switch on the growth of blood vessels to keep them nourished. The most important protein produced by cancers to encourage blood vessel growth is called vascular endothelial growth factor (VEGF). However, VEGF is made in two very similar forms, the traditionally described stimulatory form and the newly described inhibitory form. Therefore the study of VEGF's role in cancer growth and spread is not as simple as measuring the total amount, as traditionally thought, but also ascertaining the type produced.

I aim to evaluate the ratio of the stimulating and the inhibiting forms of VEGF in the normal colon and colon cancer. Furthermore, I will assess whether a surplus of the inhibitory form of VEGF can slow the growth of human colon cancer cells in animal models and if it alters the effects of anti-VEGF drug Avastin.

The vast majority of VEGF in normal colon was inhibitory, switching in two-thirds of tumours to a majority of stimulatory VEGF. Predominance of inhibitory VEGF slowed growth of human colon cancer tumours in animal models and blocked the effectiveness of Avastin therapy.

Yes, stimulatory VEGF has long been known to be a key driver of tumour growth, but only recently was it realized that there was an inhibitory form and its role in normal colon and colon cancer was unknown.

Yes, biopsies from patients treated with Avastin will be analysed for the VEGF ratio and correlated with outcome to hopefully provide a predictive biomarker of response.

If we can identify the patients whose life expectancy will increase in response to Avastin therapy (approximately 10%), then it is likely the drug will be approved by NICE for NHS use.

manipulating ATP
receptors to alter the rate of melanoma growth

Purinergic signalling in malignant melanoma

Malignant melanoma is an aggressive cancer that originates from melanocytes, the pigment-producing cells of the skin. The incidence of melanoma is increasing and the outcome for patients with advanced disease remains poor. Surgical excision remains the treatment of choice for melanoma; however, once the cancer has spread the prognosis is bleak because no anticancer drug is currently effective.

'This year over 5,000 people living in the UK will develop a melanoma skin cancer.'

Melanocytes are controlled by nerves that release chemicals altering their growth. This is because the nervous system and melanocytes develop from the same cells in the embryo. One of the substances released by the nerves is called adenosine triphosphate (ATP). ATP acts on special receptors on the surface of melanocytes and melanomas. These receptors are involved with controlling the growth of these cells.

By bridging the gap between neuroscience and cancer research I have demonstrated the presence of ATP receptors in excised specimens of melanomas and melanoma cell lines. Using five different cellular and molecular biology techniques I have shown that these receptors can be manipulated to speed up and slow down the growth of melanomas. Two receptor subtypes were identified (called the P2Y1 and P2X7 receptors). Activation of the P2Y1 receptor caused the rate of growth of the cancer to slow down and activation of the P2X7 receptor caused the cancer cells to die.

In addition, an in vivo model of melanoma was developed, which responded well to treatment with systemic ATP. Treatment of this model with ATP caused a significant reduction in the rate of growth of the cancer and prevented weight loss, which is associated with advanced cancer. P2Y1 and P2X7 receptors may prove a novel target for the treatment of melanoma and the first clinical trials of ATP as an anti-cancer agent are being established.

Fellowship/Sponsor
RCS Research Fellowship

Mr Nicholas White

Site of study
University College London

Supervisors
Prof G Burnstock

Publications

Trends in Pharmaceutical Science 2006; **27**(4): 211–217.

Cell and Tissue Research 2005; **321**(3): 411-418.

Presentations

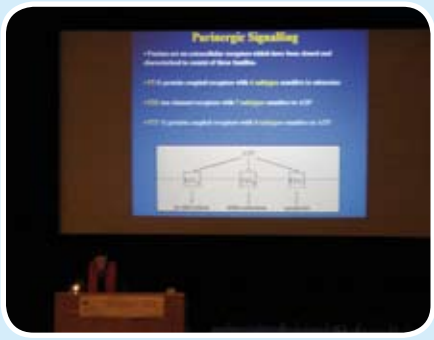
European Congress of Scientists and Plastic Surgeons, Munich

Quincentenary Scientific Congress, Edinburgh

Prizes

Arris and Gale Lecture in Anatomy and Physiology, RCSEng

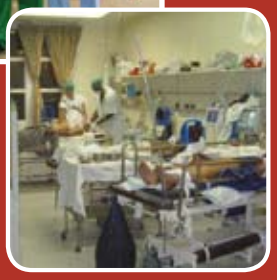
1st Place Life Sciences, University College London Annual Post-Graduate Research Competition



Delivering my Arris and Gale Lecture at The University of Sheffield during the annual British Association of Plastic, Reconstructive and Aesthetic Surgeons annual conference.

Being awarded the Arris and Gale medal by Mr Christopher Walker, President of BAPRAS, after delivering my lecture.

preiskel prize reports



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Mr Faisal Ali

Plastic Surgery Elective

Site of study: Bahawal Victoria Hospital, Bahawalpur, Pakistan

Faisal examining the hand of a young girl with a burn injury.

Faisal (left) in the operating theatre.

In March 2007, I was on elective with Dr Mughese Amin, a plastic surgeon who works in a governmental hospital in Bahawalpur (Pakistan), a provincial town in the Southern Punjab. Throughout my attachment I attended theatre lists, outpatient clinics and ward rounds, encountering a tremendous diversity of pathology, ranging from cleft lips and palates, to industrial accidents (including burns, hand amputations and 'scalpings') and traumatic injuries (including cut noses, and jaw fractures).

My learning objectives were:

1. To be able to take a focused history, perform a relevant examination and identify patients suitable for plastic and reconstructive surgery.
2. To learn about the array of techniques used in plastic surgery.
3. To consolidate my basic surgical skills such as suturing of wounds and perform procedures that might be performed by a basic surgical trainee in England.

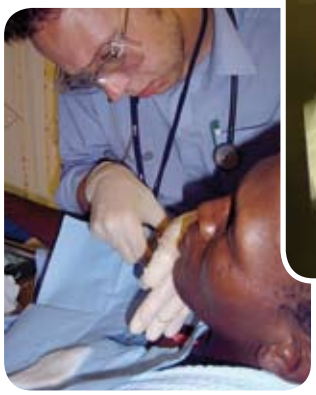
The high throughput of patients (up to 100 per outpatient clinic) and the immense variety of pathologies kept me gripped throughout my attachment. Also, there were no regular medical students doing plastic surgery attachments, so I received excellent individual tuition on a daily basis and had no competition in being the principal assistant during operations.

My elective surpassed my high expectations, fulfilled all of my original learning objectives and furthered my wish to become a plastic surgeon with an interest in craniofacial reconstruction. I very much hope to return to Bahawalpur regularly both to contribute my skills and to learn from opportunities afforded by the surfeit of practical experience. I would unreservedly recommend this attachment to any trainee wishing to gain a tremendous amount of practical experience. Finally, I would like to thank the trustees of the Preiskel Prize 2006 for assisting me financially in my elective and furthering my interest in plastic surgery.

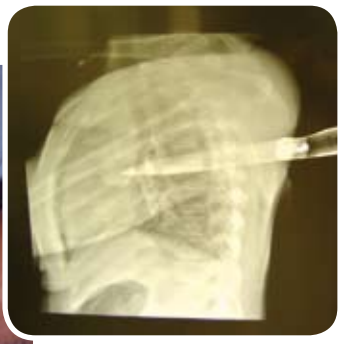
Dr Jonathan M Behar

Gunshot wounds to the chest – management and outcome: a prospective study

Site of study: Groote Schuur Hospital Trauma Unit, Cape Town, South Africa



Jonathan stitching a superficial chest wound.



Chest X-ray showing a large 6-inch kitchen knife with which this lady was stabbed in the chest by her husband. A reminder of the terrible violence affecting women in South Africa.

I worked in a busy emergency department, which received an abundance of penetrating trauma injuries. I wanted the opportunity to learn about the recognition and management of the acutely ill patient and to be able to gain experience in numerous practical procedures. I was keen to get to grips with certain pathologies and different stages of clinical disease seldom found in UK hospitals, an invaluable exposure. Ultimately I hoped to lend a helping hand, to what I understood to be an already overstretched department struggling to contain the consequences of the rise in criminal activity.

I worked in a large trauma unit with over 40 beds and its own designated resuscitation room, CT scanner and theatres. I saw patients with multiple penetrating injuries, performing lots of stitching and putting in chest drains as well as helping out with various emergency surgical procedures.

I set up a prospective study to look at the management and outcomes of patients who sustained gun shot wounds to the chest and the data collection continued after I left. I found that despite the injuries sustained, most individuals were managed with merely a chest drain and fluid resuscitation (from a drip) and only very few patients needed surgery.

My elective in South Africa was the most incredible experience of my life. It fulfilled all my objectives but went so much further. I was able to improve my clinical judgment in the management of acutely ill people and prioritise treatments in a highly charged, busy environment. I learnt and practised my suturing skills along with central line insertion – and I ended up teaching chest drain insertion by the time I left. I was certainly completely overwhelmed when I started and the first night on call was particularly daunting. But by the end I was far more competent and confident with my own assessment and management plans.

Dr Thomas J Cahill

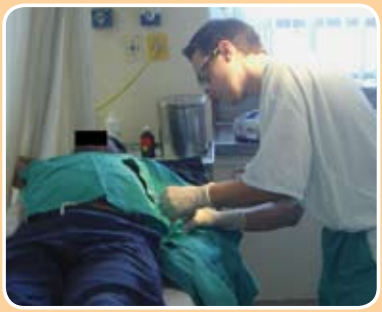
Trauma and burns in Cape Town

Site of study: Tygerberg Hospital, University of Stellenbosch, Cape Town, South Africa Red Cross Children's Hospital, University of Cape Town, South Africa

I spent my elective period in Cape Town, with the time split between the trauma surgery and burns/plastic surgery firms at Tygerberg Academic Hospital, and paediatric surgery at Red Cross Children's Hospital.

Tygerberg is a 1,400-bed tertiary referral hospital and trauma centre serving the deprived Cape Flats, a vast expanse of shanty towns sprawling out from the city centre. The trauma team perform approximately 700 trauma laparotomies per year, with stabbings, gunshot wounds and injuries from major road traffic accidents routine. I was taught and supervised inserting chest drains, central lines and closing abdominal incisions. The opportunities to assist in theatre and suture wounds in the trauma department were innumerable. At Red Cross, an international paediatric surgery centre for Southern Africa, I carried out a retrospective analysis of paediatric burns, with the future aim of formulating a preventative strategy at a public health level. I also had the opportunity to assist in skin grafting and reconstructive procedures with the plastics team as well as participating in ward work.

My elective gave me the opportunity to participate in the management of patients at a level beyond what is generally possible for medical students in the UK. The close supervision and strong teaching ethos meant that my understanding of trauma resuscitation and management, and basic surgical skills have improved greatly. I would highly recommend spending time in South Africa to anyone considering a surgical career.



Suturing in the trauma department.

Inserting a chest drain in resus.

Anoma Lalani Dias

A study examining the efficacy of the management of surgical emergencies at the Teule Hospital, Muheza, Tanzania

Site of study: Teule District Designated Hospital, Teule, Muheza, Tanzania

Lalani suturing, assisting in an emergency hernia operation.

I spent my elective period working in the surgical wards and operating theatre of the Teule Hospital, a busy 260-bed rural hospital in Tanzania serving a catchment population of 280,000. While there, I started a prospective 5-year study investigating the management of acute abdominal surgical emergencies since these formed the majority of emergency surgical admissions.

In many developing countries of the world the need for surgical treatment of acute abdominal emergencies is largely unmet. Patients attending the Teule hospital have most often travelled from far outside the Muheza district and are therefore likely to be susceptible to late diagnosis and adverse outcome. Whereas there is little that can be done before patients present to hospital, once they do present, there are several parameters that can affect outcome.

The aim of this study was to present the experience of surgery for acute abdominal conditions in this population and to assess various parameters eg time to diagnosis, operative contamination, in order to identify how and where clinical outcome was affected. This was done using a proforma assessing parameters pre-operatively, operatively and post-operatively, which was completed for each acute emergency surgical admission fulfilling the study criteria.

Various difficulties encountered during the management would be highlighted and measures to overcome these problems sought. The study is currently ongoing but already we have been able to draw attention to areas where errors and delays to surgery frequently occurred, identifying how these could be remedied and prevented. This will undoubtedly benefit patient care and overall outcome.

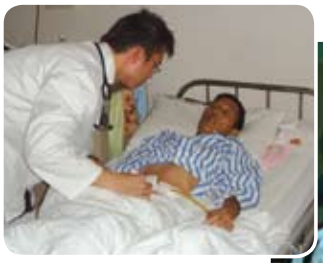
Whilst at the Teule hospital I was also involved in the day-to-day clinical work which involved ward work, clinic and theatre duties. I had the opportunity to look after my own set of patients, often with varied clinical presentations or advanced disease and assist in many operations. I feel that these greatly improved my diagnostic and clinical surgical skills.

Lalani suturing, assisting in an emergency amputation operation.

Chee Lin Gan

The Surgical Management of Colorectal Cancer

Site of study: The First Affiliated Hospital College of Medicine, Zhejiang University, Hangzhou, China



Post-operative examination of a patient with bowel resection.

Assisting in an operation.

I spent my elective period in the colorectal surgery department in the hospital. The aims were to improve my knowledge of different techniques of colorectal surgery, focusing on colorectal cancer, and to appreciate the differences in practice between China and UK.

In China, there is an increasing incidence of colorectal cancer among the population. I have always had a special interest in colorectal surgery and the fact that I am fluent in Mandarin had inspired me to do this project in the biggest hospital in the Zhejiang Province.

Not only did I get to assist many different colorectal operations, I also had ample opportunity to take an active role in pre-operative assessment and post-operative management of the patients. I was particularly fascinated by the advanced, highly effective but expensive anastomotic techniques used, which I have not come across in Wales.

They have also developed a new anastomotic technique using male sterile condom but the technique was still under trial and I was able to contribute in writing up this research article. I had the opportunity to perform the colonoscopy on five relatively young and healthy patients selected by my supervisor under supervision. I managed to detect and remove polyps using the loop diathermy, as well as taking biopsies from the bowel endoscopically.

After assisting in many haemorrhoid repair operations, I was given the opportunity to perform such an operation, under close supervision by my supervisor, using the latest procedure for prolapse and haemorrhoids (PPH) technique which was fast, simple but expensive and is currently not available in NHS Wales.

I benefited a lot from the one-to-one teaching from professors and the hands-on experience in many procedures and operations. This experience has strengthened my desire to be a surgeon in future. The hospital system in China is drastically different from the NHS hospital system and I would definitely recommend this elective to all medical students.

Dr Esther Wangui Gathura

Paediatric surgery in the developing world

Site of study: Kijabe Mission Hospital. Kijabe, Kenya

Children suffering with hydrocephalus, who had surgery at the hospital.

I carried out my placement at Bethany Kids at Kijabe hospital (BKKH), a rural Hospital in Kenya. This paediatric referral centre is involved in providing corrective surgical care to children with physical disabilities, parent support and refugee work.

My main objective during the trip was to gain insight into common paediatric orthopaedic conditions that present in the developing world setting, and learn how they are managed in the backdrop of limited resources. I was able to observe and assist in the clinical assessment of children with spina bifida (congenital deformity of the back causing paralysis) and cerebral palsy following hydrocephalus (increase in the cerebral spinal fluid within its main containing structure, the ventricle). This included performing and interpreting cranial ultrasound scans and performing cerebral spinal fluid taps. I had opportunity to observe endoscopic brain surgery, insertion of cerebral spinal fluid shunts and management of spina bifida. Other commonly encountered conditions were clubfeet, burn contractures, and general paediatric surgical conditions like hypospadius and hernias.

Conceivably, my main achievement during this placement was carrying out an audit aimed at reviewing complications and outcome following the management of hydrocephalus by use of cerebral spinal fluid shunts (CSF shunts) in 574 cases performed between the year 2004 and 2006 at BKKH. This surgical procedure is associated with high complication rates, and in the developing world, malnutrition, HIV and lack of adequate resources make the use of this treatment challenging. Encouraging results from this study showed lower complication rates and reasonable outcome, contrary to results reported by previous studies carried out similar settings.

I learnt that spina bifida and congenital foot deformities, as well as the frequent complication of spina bifida and hydrocephlalus, which also occurs after meningitis, are frequent conditions in this setting and that their management is often inextricably linked. For an aspiring paediatric orthopaedic surgeon aiming to practice in Kenya, this experience was particularly insightful.

Rishikaisan Gnaanachelvan

The surgical workload and effectiveness of the provision of healthcare services based on financial resources compared with the UK

Site of study: Sri Sathya Sai General Hospital, Bangalore, India

My elective was based at the Sri Sathya Sai General Hospital (SSSGH). The outpatient department treats around 500 patients a day. Three operation theatres in the hospital handle around 15 surgeries daily and an average of 35 inpatients are admitted every day. This hospital was unique in that patients were treated free of charge, ideal for a society which did not have the financial resources for investing in even their basic healthcare, much of which we in the West take for granted. The hospital relied on the donations of devotees of an Indian spiritual guru, Sri Sathya Sai Baba. One thing that was clear to me early on in my elective was that the hospital's success rested strongly on its volunteers being driven by a high degree of commitment and service orientation. This has produced hospitals of remarkable financial efficiency and work ethics in the third world, while providing a first-class service to patients and ensuring their utmost satisfaction.

The aim of my elective was to experience plastic surgery as a tool necessary to improve functionality, quite contrary to the stereotypical perception of glorified images of breast augmentations, facelifts and other fancy cosmetic surgeries. I came across numerous surgical cases including post-op cleft repairs, keloids, basal cell carcinomas (often at a clinically late stage of presentation), lipomas, post-burn contractures and various reconstructive procedures.

An institution such as the SSSGH, providing free, quality medical care to people from economically less privileged strata is important and value-creating and helps to address the issue of inequity in healthcare access. Such healthcare becomes increasingly necessary in a developing country for 'the wealth of a nation lies in the health of its people'.

Rishi (left) with the surgeons.

Rishi in the operating theatre.

Emily Kidgell

Western surgeons a long way from home – a surgical elective in Cambodia

Site of study: A mission in Siem Reap, Cambodia and Chey Chumneas Hospital, Kandal Province on the outskirts of Phnom Penh

In August 2006 I travelled to Cambodia to spend my elective learning about surgery. Under the name Operation Smile, a team of Canadian and American surgeons fly to Cambodia annually to teach and assist the Cambodian surgeons in a week of operating. The bulk of the caseload is cleft lip and palate repairs. I accompanied my supervisor, Dr Nous Sarom (a Cambodian plastic surgeon) to a mission in Siem Reap. Once the mission was complete, I undertook the rest of my elective at Chey Chumneas hospital in the Kandal Province on the outskirts of Phnom Penh. There I participated in day-to-day emergency general surgery, working on the wards and in theatre.

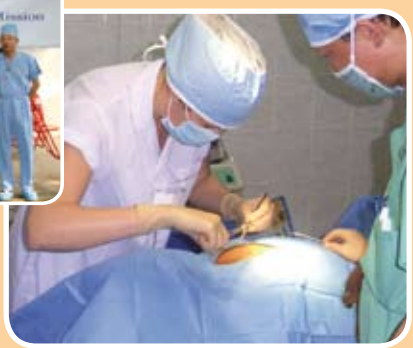
Taking Operation Smile as an example, my research aim was to investigate the role of the non-governmental organisations (NGOS) in a developing country and in particular find some reassurance that these surgeons are making a long-term difference to their patients. I fulfilled this by tackling the following two objectives:

- Determining the follow-up services available after surgery
- Interviewing post-operative patients to obtain their perspective

Very simply, there was no formal follow-up after surgery. The responsibility fell onto the local Cambodian surgeons to deal with any complications that may present. It appears that this area of NGO surgery is often underfunded. Talking to patients (via an interpreter) was a particularly interesting experience. Patients were generally worried about admission to hospital, but unsurprisingly had nothing but praise for the surgical team.

Operating for a surgical NGO has always appealed to me. I was inspired to undertake this elective by previous medical student reports. I would certainly recommend an elective in developing world surgery; it is an absorbing, sometimes scary yet invaluable experience.

Emily (2nd from the left) with some of the Operation Smile Team.



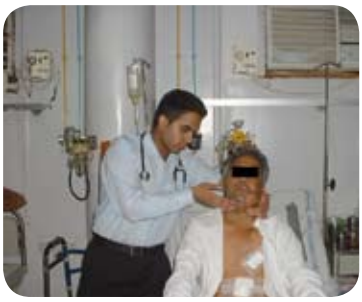
Emily suturing after an excision of a large neurofibroma, supervised by an Operation Smile surgeon.

Dayal Mukherjee

Surgical management of head and neck neoplasms in South Asia

Site of study: Tata Memorial Hospital, Mumbai, India

Some time for relaxation.



Dayal examining a patient's neck after his operation.

The habit of 'betel quid' chewing was noted by the Portuguese when they arrived in the Philippines in 1521. The betel (or areca) nut constitutes a local irritant to the oral mucosa that predisposes to the development of cancers of the head and neck. By 1521, however, this traditional habit had existed in South and South East Asia for over 2000 years, a legacy responsible for the Herculean public health concern this carcinogenic addiction now presents to India and its neighbouring countries. My aim was to gain clinical exposure to the surgical management of these head and neck cancers in the setting of a developing country with limited resources but a huge patient load.

My elective was spent at the Tate Memorial Hospital Mumbai, India, under the care of Professor Anil D'Cruz, one of the leading head and neck oncological surgeons in South Asia who, despite being extremely busy, took the effort of continuously addressing my needs and expectations from the elective. Generally speaking, my time on the attachment was divided between seeing pre- and post-operative patients on the wards and in outpatients, attending theatre to observe some fascinating surgery and spending time trying to amass data for my audit. Over 1,000 patients visit Tata's outpatient clinics daily. The highly technical surgical procedures I observed included radical neck dissections and laryngeal tumour resection. It was remarkable that every patient with oral cancer I examined had chewed betel nut for some period in the past and this observation is reflected in national statistics.

Being fluent in two Indian languages, Hindi and Bengali, was a great advantage to me in my work, in a way that I was able to contribute effectively to patient care.

It was a humbling experience to observe the work of the best cancer surgeons in India, who have made Tata Memorial a centre of excellence in a much more difficult work environment than the one I am used to in London.

Sanjeeva Pathmanathan

Elective in trauma surgery in South Africa

Site of study: Chris Hani Baragwanath Hospital, Johannesburg, South Africa

Standard uniform for all trauma doctors at Bara.

I chose to work in Bara Hospital because I have a keen interest in trauma surgery. On arrival I was given a uniform, orientated around the hospital and put onto the work rota as well as on-call timetable. My work covered wards round and ward work, assisting in theatre and working in the 'surgical pit', the surgical section of the emergency room. I also had to attend the morning hand-over meetings, mortality meetings, X-ray teaching and specialist teaching on areas such as managing penetrating injuries to the neck, crush injuries to the pelvis, etc. Most of the teaching was very practical and aimed at common cases that would enter the department.

A lot is expected of the students who are here on elective and it is on a par to a real job. The hours are very long and tiring, but if this is a field that you are interested in then you will learn a huge amount.

Everyone was very keen to teach and you are able to get hands-on experience of procedures, ie suturing, chest drains, resuscitation, etc.

It is an ideal place to develop confidence in yourself and the ability to stay calm. Regardless of injury that comes through the door, you learn that in every case A,B,C,D,E (from the ATLS® course) works and gets you through. I found there to be an exceptionally steep learning curve and a lot of emphasis is put on students who have been there for a while to show you how things work; you in turn pass it on to those who follow. Initially I did feel out of my depth but you do adapt to your surroundings. You are also expected to assist in theatre and there are opportunities to ride along in the rapid response car and ambulance.

I left having learned a lot about surgery and even more about myself. You will witness and manage pathology and trauma of such volume and intensity that you would never experience in England. It is somewhere I would definitely return to for a sabbatical year, hopefully after commencing on a surgical training programme in England.

Iestyn Shapey

Trauma surgery

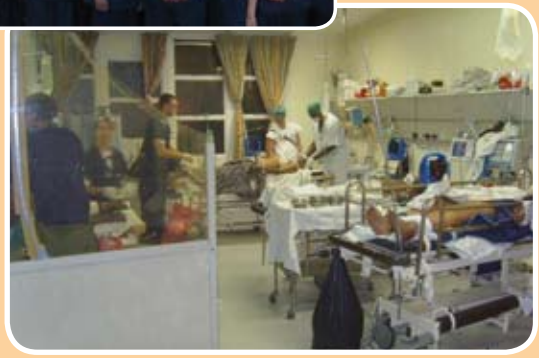
Site of study: Trauma Unit, Chris Hani Baragwanath Hospital, Soweto, Johannesburg, South Africa

Chris Hani Baragwanath Hospital (Bara), a 3,000-bed tertiary referral centre, is located in one of Johannesburg's largest townships, Soweto, and is the largest hospital in the southern hemisphere. Formerly a military hospital, its physical structure can, at best, be described as basic; however, the teamwork, dedication, and resourcefulness of its doctors and nurses is nothing short of inspiring.

The Bara trauma unit sees an extremely high volume of patients: gunshot wounds, stabbings, and motor vehicle accidents comprise the majority of the workload. With such a lot to do, a great deal of work and effort was expected from the elective students and a regular commitment to an ever-busy 24-hour call, along with ward work and assisting in theatre was rewarded with many opportunities to learn and practice many valuable skills. These newly learnt skills were essential in light of the responsibility that was bestowed upon students to contribute to patient care when (as often was the case over a weekend) a full resuscitation room meant scores of stretchers lined up outside waiting for attention.

It was also very interesting to be part of a team where the care of any traumatic injury was under the remit of the trauma unit, as opposed to requesting the skills of different specialties (such as cardiothoracics to treat injuries of the heart, lungs and great vessels, or urology to repair, for example, ruptures of the bladder). This meant that the team would be performing a broad range of operations in every region of the body, and that the doctors were highly skilled and capable of dealing with anything that came through the door.

The Trauma Team.
Iestyn: 3rd row, 3rd from the right.

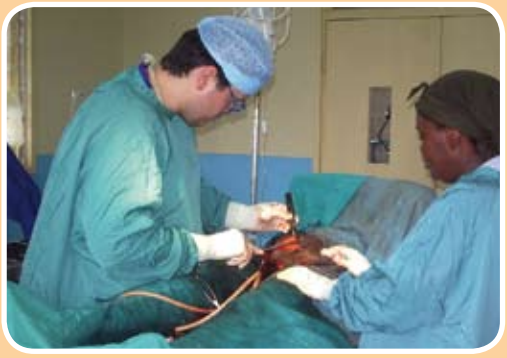


The resuscitation room on a weekend night.

Paul Sutton

Trauma and general surgery in Africa

Site of study: Department of Trauma, Groote Schuur Hospital, Cape Town, South Africa and Teule Hospital, Muheza, Tanga Region, Tanzania



Paul closing after performing his first Caesarean section.

I spent four weeks in the department of trauma at the Groote Schuur Hospital in Cape Town, the largest trauma department in the Cape. The department sees an average of 117 patients per day, comprising 49% penetrating trauma, 38% blunt trauma, 7% falls and 6% other injuries.

My time in the department was split between working in the 'front room', where the trauma patients are received, and in the trauma theatre. While in the front room I managed a number of patients, ranging from the critically ill to walking wounded, and also learned a number of practical procedures. My confidence in managing critical patients increased exponentially, as due to the staffing levels I was frequently left on my own to manage patients that in the UK would have had the whole trauma team! While in the trauma theatre I received some excellent tutorage from the trauma surgeons and again my surgical skill increased dramatically.

The second four weeks of my elective were spent at Teule hospital, a small district designated hospital on the west coast of Tanzania. It has 180 beds, frequently occupied by two patients in the adult wards and three patients in the paediatric wards. There is also a busy outpatient department with an average clinic attendance of over 100 patients.

While I spent the majority of my time with the surgical team in theatre, there was a great deal of need for staff on the wards. My role was to perform the daily ward rounds with the nursing staff, including seeing the paediatric patients. Teaching was an important element of the rounds that we did and I hope that the time I committed to this is continuing to help the patients there even today. I was also fortunate enough to be involved in an HIV patient education programme, and helped to build the new theatre complex at the hospital.

Paul doing the surgical ward round.

Jignesh Tailor

Management of head injury in Papua New Guinea

Site of study: Port Moresby General Hospital, Papua New Guinea

I spent my elective in the general surgical department of a university hospital in Papua New Guinea under the supervision of the only general surgeon trained in neurosurgery in the country. I wanted to see the variety of neurosurgical cases in a developing country and how traumatic brain injury was managed in the face of limited resources.

Papua New Guinea has a high incidence of trauma. The mechanism of head injury was diverse and included assaults, spear injuries and falls from mango trees. I was actively involved in the management of these cases and was fascinated to learn how intracranial haematomas were clinically diagnosed and evacuated in the absence of brain imaging or intensive care monitoring devices.

This elective gave me an unforgettable insight into the practical realities of neurosurgical practice in the developing world: in particular, the difficulties in transferring patients with severe head injuries to hospital from remote places, the surgical exploration of the skull for haematomas in the absence of a brain scan and the improvisation of central venous pressure monitors in the intensive care unit. My research focused on how one could estimate intracranial pressure after head injury with the limited resources available. This involved a review of the early intracranial pressure monitors.

Jignesh exploring an arrow wound in the neck.

Jignesh (far left) with his supervising consultant and registrar on the surgical ward.

Hunterian, Arris and Gale, Arnott

lectures delivered in 2006 and 2007

2006

Arris and Gale **Mr Marcus Drake,** BAUS, Manchester, 28 June 2006
The integrative physiology of the normal detrusor and a unifying hypothesis of detrusor overactivity

Hunterian **Miss Emma Barker,** BAO-HNS, Birmingham, 5 July 2006
Ischaemic and immunological injury in a laryngeal transplant

Hunterian **Mr Rami Salib,** BAO-HNS, Birmingham, 5 July 2006
Transforming growth factor-beta in allergic rhinitis

Hunterian **Mr Oliver Jones,** ACPGBI, Gateshead, 6 July 2006
Towards safer treatments of benign anorectal diseases: the pharmacological manipulation of the internal anal sphincter

Hunterian **Mr Shehan Hettiaratchy,** BAPRAS, Sheffield, 12 July 2006
A preclinical model of allogenic reconstructive transplantation without long term immunosuppression

Arris and Gale **Mr Nicholas White,** BAPRAS, Sheffield, 14 July 2006
Extracelluar nucleotides regulate the growth of melanomas

Hunterian **Miss Archana Vats,** BAO-HNS, London, 7 September 2006
Tissue Engineering and Stem Cells: Chondrogenic differentiation of Human Embryonic Stem Cells

Hunterian **Mr Mark Rochester,** BPG, Cardiff, 7 September 2006
Silence of the Genes – Developing novel molecular therapy for prostate cancer

Hunterian **Mr Timothy Briggs,** BOA, Glasgow, 27 September 2006
Autologous chondrocyte implantation of the knee – clinical outcome, and histological assessment in a prospective study with follow-up of 8 years

Hunterian **Mr Robert Mulholland,** BOA, Glasgow, 28 September 2006
The scientific basis for the surgical treatment of low back pain

Arnott **Mr Benjamin Turney,** RCS, London, 13 November 2006
Anatomy in a Modern Curriculum

Hunterian **Mr Jonathan Lund,** Derby City General Hospital, Medical School, 16 November 2006
Aetiology and Treatment of Anal Fissure.

Hunterian **Professor John Shepherd,** BASO, London, 27 November 2006
Challenging dogma: radical conservation surgery for early stage cervical cancer in order to retain fertility

Hunterian **Mr Matthew Potter,** BAPRAS, London, 6 December 2006
Transforming the treatment of burns with a proangiogenic skin substitute, a new paradigm in the management of large wounds

Hunterian **Mr Rowan Pritchard Jones,** BAPRAS, London, 8 December 2006
VEGF165b - an endogenous anti-angiogenic agent with therapeutic and prognostic potential for patients with malignant melanoma

2007

Hunterian **Mr Robert Longman,** RSM – Section of Coloproctology, Middlesex, 16 March 2007
Component expression of the colorectal mucosal defence barrier in disease

Hunterian **Miss Polly King,** ASGBI, Manchester, 19 April 2007
Enhancing recovery after surgery for Colorectal Cancer

Hunterian **Mr Amjid Riaz,** ACPGBI, Glasgow, 3 July 2007
The role of leukocytes in inflammatory conditions of the colon

Hunterian **Mr Ian Daniels,** ACPGBI, Glasgow, 4 July 2007
Targeting treatment in rectal cancer: The optimal use of pre-operative staging

Hunterian **Mr Christopher Hobbs,** BAO-HNS/RSM, London, 6 September 2007
MHC, HPV and HNSCC – The Good, the Bad and the Ugly

Hunterian **Mr Mustaque Ishaque,** BOA, Manchester, 26 September 2007
The genetic basis of lumbar disc degeneration and low back pain

Hunterian **Mr John Newman,** BOA, Manchester, 28 September 2007
Contributions to the cause of compartmental Knee Replacement

fundraising in focus

Our Partners

Since the launch of the scheme in 1993, over 400 fellowships have been awarded to innovative programmes throughout the UK. Each fellowship is selected to resolve long-standing clinical problems and fellowships have included a wide range of surgical specialties, covering topics such as gene therapy for head and neck cancer, heart transplantation and the debilitating disease, rheumatoid arthritis.

The success of the College's surgical research fellowship scheme would not be possible without the loyalty and generosity of our funding partners; charitable trusts, companies and individuals who share in our aim of securing improvements in patient care and recovery.

Our Events:

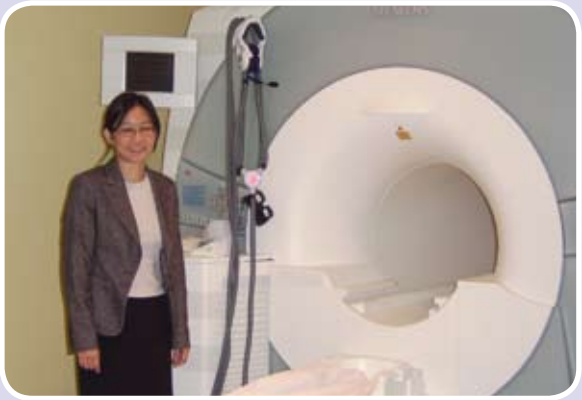
The College continues to organise events to highlight the work of our research fellows. Over the past two years four research evenings have been held at the College and a further twelve presentations to Women's Institutes, Freemasons Lodges and other national groups across the United Kingdom. These events are invaluable in communicating to our donors and the wider public the results of ground-breaking research supported through this scheme.

The College would like to acknowledge its gratitude to Hywel Jones for his hard work and give him all best wishes for the future.

The Dunhill Medical Trust (DMT) is delighted to be able to work in partnership with the College by supporting five research fellowships in surgery related to diseases of ageing and older people. One of DMT's key objectives is to support activities aimed at expanding research capacity among clinicians and scientists and our long-standing relationship with the College has helped to fulfill this. Teaming up with the College has meant that we have had access to the most talented young surgeons in the country and have been able to provide them with an opportunity to take time out of their specialist training to gain valuable experience of rigorous research and research methods, which will enhance their future careers as well as contributing to the sum of surgical knowledge.

Claire Large, Administrative Director

Research Evening at The Royal College of Surgeons of England.



Dunhill Medical Trust Research Fellow Nicole Keong.

The College, surgeons and patients have every reason to be grateful to them

fundraising in focus

The College would like to acknowledge all those charitable trusts, companies, College fellows and individuals who have supported surgical research at the College, including:

Dental Science Fund
Sunley Fund for Hunterian Institute
PKK Award

Foundations/Charitable Trusts/ Corporate donations/Individuals

Andrew Anderson Charitable Trust
Ballinger Charitable Trust
Blond McIndoe Medical Research Trust
The Caravan Club (Suffolk Centre)
Cazenove Charitable Trust
Mr Eion Crighton
Dunhill Medical Trust
East Grinstead Medical Research Trust
Enid Linder Foundation
Ethicon UK Ltd
Euclid Lodge of Installed Masters
Family Rich Charities Trust
Fellows Fellowship Fund – *The College is very grateful to its many members and fellows who donate regularly to the fellowship scheme*
Frances & Augustus Newman Foundation
The Family of the late Mr Stefan Galeski FRCS
George Drexler Foundation
Grand Lodge of Freemasons 250th Anniversary Fund
Henry Smith Charity
Herefordshire Masonic Charity Association
Mrs Bella Hopewell
Kirby Laing Foundation
Lodge of Academe No 9337
Mr REW Lumley
Rosetrees Charitable Trust
Shears Charitable Trust
Thomas Sivewright Catto Charitable Settlement
Vandervell Foundation
Warwickshire Installed Masters Lodge
Wyndham Charitable Trust
W D Macpherson Trust

Joint Fellowships

British Association of Plastic, Reconstructive and Aesthetic Surgeons
British Scoliosis Research Foundation
Cancer Research UK
CORE
Society of Academic & Research Surgeons
The American College of Surgeons
The Arthritis Research Campaign
The Botnar Family
British Society for Surgery of the Hand
The Healing Foundation
Ia – The Ileostomy & Internal Pouch Support Group
The Medical Research Council
The National Kidney Research Fund
The Restoration of Appearance and Function Trust
The Royal Australasian College of Surgeons
The Stroke Association
Welsh Surgical Society

Prizes and Awards

Ethicon Foundation Award
Lionel Colledge Memorial Fund
Sir Ratanji Dalal Research Scholarship
MacLoughlin & Morris Scholarship
Norman Capener Travelling Fellowship
The Preiskel Prize
Ronald Raven Barber's Award
H J Windsor Prize

Endowments and Legacy Funds

Anderson Reid Fund
Bennett Legacy
Bernhard Baron Fund
Bingley Legacy
Brinsdon Legacy
Buckston Browne Gift
Burghard Bequest
Cameron Legacy
Campbell Legacy
Children with Cancer Research Fund
Clark Legacy
L M Coleman Legacy
Collett Legacy
Philip & Lydia Cutner Bequest
Darlow Research Fellowship
Denker Legacy for Research in the UK
Edward Lumley Fund
Ellin Legacy
Fletcher Legacy
George Clarke Bequest
Gerrish Legacy
Green Legacy
Grimwood Legacy
Grossman Legacy
Guyatt Legacy – Sir Alan Parks Research Fellowship
Harold Bridges Bequest
Harry S Morton Fund
Heslop Legacy
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James Kent Will Trust
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Kathleen Knapp Legacy
Kennard Legacy
D K King Legacy
Knapp Legacy
Laming Evans Research Fund
Lea Thomas Fund
Lillian May Coleman Fund
Louis Alexander Research Fellowship
Maynard Legacy
Muirhead Bequest
Osman Hill Collection and Research
Parks Visitorship
Phillips Legacy
Phillips, P I Legacy
Prophit Trust
Robb Legacy
Seargeant Research Fund
The Dr Shapurji H Modi Memorial ENT Research Fund
Shortland Legacy
Simpson Legacy
Sir Arthur Sims Fund
Sir John Lang Bequest
The estate of the late Dr M P Starritt
Taylor Legacy
Tudor Edwards Fellowship
Vandervell Research Fund
Watts Legacy
Williams Legacy

If you would like further information about how to make a donation to Surgical Research Fellowship Scheme, or holding events in your area, **please contact the Development Office on 020 7869 6083 or development@rcseng.ac.uk**

travelling fellowship awards

The College is pleased to be able to offer a variety of awards as a result of the generous support of companies and individuals. These awards give surgeons the opportunity to work in an overseas institution to learn more about a particular surgical technique or area. The main benefit of the travelling awards is that the surgeon who benefits can translate the experience and know-how gained during the overseas fellowship to his or her own knowledge base, to benefit future patients in this country. The committees that decide the recipients of the travelling awards always include leading surgeons.

The following Travel Awards are available:

Ethicon Foundation Fund Travel Award

The Ethicon Foundation Fund was established by the generosity of Ethicon Limited. The Fund provides financial assistance towards the cost of the travel to and from a research or training fellowship, thereby promoting international goodwill in surgery. Applicants should be sufficiently advanced in their training to benefit from such an experience or be within one year of their appointment as consultant surgeon.

Recipients

May 2006

Miss Helen Cocks, *Vrije Universiteit Medical Center, Holland*
Mr Richard Justin Davies, *University of Toronto, Canada*
Mr Giles Hellawell, *The Monash Medical Centre, Victoria, Australia*
Mr Oliver Jones, *Royal Brisbane Hospital, Australia*
Mr Paul Latimer, *Royal Perth Hospital, Australia*
Mr Christopher Pring, *Royal Brisbane Hospital, Australia*
Mr Henry Wynn-Jones, *Beit Cure International Hospital, Malawi*

September 2006

Mr Daren Forward, *R Adams Cowley Shock Trauma Unit, USA*
Miss Celia Larcombe, *Queen Elizabeth Hospital, Blantyre, Malawi*

April 2007

Ms Emma Barker, *Princess Margaret Hospital, Toronto, Canada*
Miss Caroline Burt, *Mount Sinai/Toronto General & St Michaels Hospital*
Miss Joanne Cresswell, *Klinikum Heilbronn, Germany*
Ms Jeevendra Kanagalingam, *Princess Alexandra Hospital, Brisbane, Australia*
Mr James Ramsden, *University Hospital Network, Toronto, Canada*
Ms Emma Sidebotham, *Memorial Sloan-Kettering Cancer Centre, New York*
Ms Stephanie Symons, *Muljibhai Patel Urological Hospital, Nadiad, India*
Mr Nikesh Thiruchelvam, *Royal Perth Hospital, Perth, Australia*
Mr Matthew Trotter, *Royal Victorian Eye and Ear Hospital, Australia*
Mr Gregory Wynn, *Pamela Youde Nethersole Eastern Hospital, Hong Kong, China*

The Lionel Colledge Memorial Travelling Fellowship

The Lionel Colledge Memorial Travelling Fellowship was established by Miss Cecilia Colledge in 1979 in memory of her father, the distinguished surgeon Lionel Colledge. The Fellowship was founded to promote and advance the study and knowledge of surgery, in particular head and neck surgery, for the benefit of patients. Applicants must be senior trainees or new consultants and plan to a study for a period overseas. Miss Colledge remains a trustee of the fund and takes an active interest in its activities.

Recipients

2006

Miss Emma Barker, *The Princess Margaret Hospital, Canada*
Miss Nneka Eze, *Fowler Institute, Columbia University, New York, USA*

2007

Mr James Daniel Ramsden, *Toronto General Hospital, Toronto Sick Kids and Markham Stouffville Hospital, Canada*
Mr Carl Martin Philpott, *St Paul's Sinus Centre, Vancouver, Canada*
Mr Matthew Ian Trotter, *Royal Victorian Eye and Ear Hospital, Melbourne, Australia*

Sir Ratanji Dalal Research Scholarship

This research scholarship was founded under the will of Sir Ratanji Dinshaw Dalal. It is awarded jointly by The Royal College of Surgeons of England and the Royal College of Physicians of London. Applications are invited for this research scholarship, which is intended to support a project in either tropical surgery or tropical medicine. The scholarship is tenable for one year and is open to all medical practitioners registered in any part of the Commonwealth. It may be held in any institution in Britain or overseas that is approved by The Royal College of Surgeons of England and the Royal College of Physicians of London.

Recipients

2006

Ms Verona Beckles, *Beit Trust Cure International Hospital, Malawi*

Mr Henry Wynn Jones, *Beit Trust Cure International Hospital, Malawi*

Norman Capener Travelling Fellowship

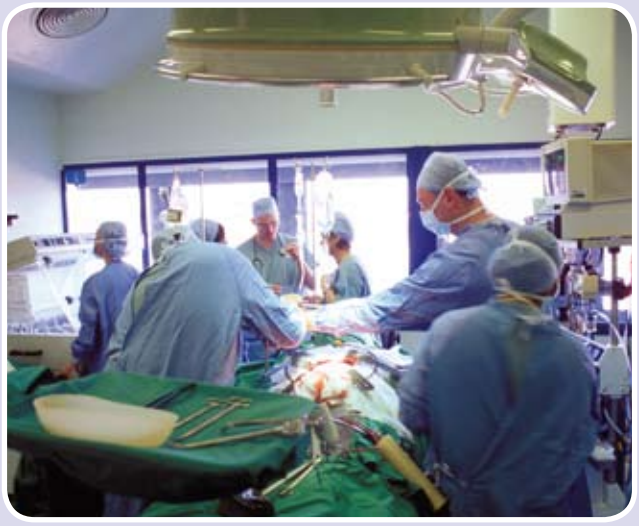
This biennial travelling fellowship was founded with funding provided by friends and admirers of the late Norman Capener a past vice-president and honorary medallist of the College. Applicants should be enrolled for orthopaedic surgical training or have recently completed a course in orthopaedic or hand surgery.

Recipients

2007

Mr Daren Forward, *R Adams Cowley Shock Trauma Unit, Baltimore, USA*

Mr Satish Kutty, *Hospital for special surgery, New York, USA*



H J Windsor Prize

The H J Windsor prize was established in 1975 with a gift from the late Dr HJ Windsor of Brisbane, Australia. The prize is intended to assist in the advancement of surgery by an annual prize for research or educational project in Australia or the British Isles.

Recipient

2006

Mr Ben Davies, *The Royal Children's Hospital, Melbourne, Australia*

Ronald Raven Barber's Award

The Ronald Raven Barbers award was established by the generosity of The Worshipful Company of Barbers (at Ronald Raven's bequest). The award is aimed at assisting trainee surgeons going abroad to develop their individual skills by special education or training of an innovative nature. Particular weight is given to the excellence of the applicant, the innovative qualities of the work to be done and the relevance of such work to the ultimate benefit of patient care.

Recipients

2005

Mr Gurdeep Biring

Mr Winston Kim

2006

Mr Hu Liang Low

Mr Richard Davies

Mr Mushtaque Ishaque

2007

Mr Robert Freeman

Mr Mark Cartmell.

Raven Barbers' Award

Fellowship/Sponsor
Raven Barbers' Award – The Worshipful Company of Barbers

Mr Gurdeep Singh Biring

Site of study
Vancouver General & Health Sciences Centre

Supervisors
Dr Bas Masri
Dr Donald Garbuz
Dr Nelson Greidanus
Professor Clive Duncan


Professor Clive Duncan.

Presentations

The Hip Society, US, 2006

British Hip Society, Leeds, 2007

Predictors of quality of life outcomes after revision total hip replacement

The number of revision hip replacements carried out in the UK comprises approximately 10% of those undergoing jointreplacement. It is more difficult than primary surgery and the outcomes not as good. It is essential to find out which factors play an important role in the outcome of this type of surgery.

This study seeks to define what the quality of life outcomes are and what factors are predictive of outcome allowing identification of patients who would benefit and identify those in whom there may be a problem so that realistic expectations can be set.

A prospective cohort of 222 patients who underwent revision hip arthroplasty was evaluated. Statistical analyses were performed to identify factors that predict quality of life outcomes (WOMAC function & pain and UCLA activity) at 1 and 2 years post surgery.

There was a significant improvement in all patient quality of life scores from baseline with results plateauing at 1 year.

In the predictive model:

- higher baseline WOMAC function, age between 60-70, male gender, lower Charnley class and diagnosis of aseptic loosening were significant predictors of improved function.
- higher baseline WOMAC function, age between 60-70, male gender, lower Charnley class and having had no previous revisions were significant predictors of improved pain scores. Baseline WOMAC pain did not predict final pain outcome.
- Baseline WOMAC function and the indication for the operation were significant predictors of UCLA activity at follow up.
- Peri or post-operative complications were not an adverse predictor of physical function, pain or activity.

Predictors of quality of life outcomes after revision hip replacement showed that although some patient specific and surgical specific variables were important, age, gender, Charnley class and baseline WOMAC function had the most robust associations with outcomes.

'Predictors Of Improved Quality Of Life Outcomes Identified After Revision Hip Replacement.'


Vancouver General & Health Sciences Centre with snow-capped mountains of Cypress and Grouse in the distance.

Clinical Effectiveness Unit

Jan van der Meulen, Director

Jan Van der Meulen with Director of LSHTM Professor Sir Andrew Haines.

The Clinical Effectiveness Unit (CEU) is a collaboration of The Royal College of Surgeons of England and the London School of Hygiene and Tropical Medicine. The unit is involved in a number of national studies of the quality of surgical care. A general characteristic of most of these projects is that they try to get a better understanding of the determinants of variations in process and outcome of surgical care. As such, they can be considered as clinical epidemiological research.

In 2006, the CEU started two national cancer audits in partnership with The Information Centre for health and social care and a number of surgical specialist organisations (National Oesophago-gastric Cancer Audit, and Mastectomy and breast reconstruction audit). These audits are funded by the Healthcare Commission and aim to produce their final reports in 2010.

Another new large project is the audit of outcomes of elective surgery provided by treatment centres run by the independent sector. This project will collect clinical information reported by the surgeons as well as information on outcomes directly provided by the patients. It aims to provide a direct comparison of the quality of care provided by these treatment centres with that of conventional NHS facilities.

The unit also continues to be a major partner in other national projects, such as the UK and Ireland Liver Transplant and the UK Cardiothoracic Transplant Audits funded by the National Commissioning Group, the CRANE Database (a database of all babies born with cleft lips and palates in the UK as well as the treatment they receive) funded by NHS commissioners, the PROMS project (a feasibility study of collecting patient reported outcome measures after elective surgery) funded by the Department of Health's Economic and Operational Research Division, and the REFER project (a project developing guidelines for the referral of patients from primary to secondary care for elective surgery) funded by the National Institute for Health Research Service Delivery and Organisation Programme. In addition, the Unit is also supporting the analysis of data collected by the National Joint Registry funded by the Department of Health (a database of all hip and knee replacements carried out in England and Wales).

Alongside these national audit projects, the unit aims to contribute to the development of methods to evaluate and monitor outcomes of surgical care. Publications regarding the value of the hospital episode statistics database, methods to identify and adjust for comorbidity, and the accuracy of prognostic models are examples of this methodological work.

The unit also organised two three-day courses in statistical methods and one two-day course in research methodology for surgeons. A special feature of these courses is that they aim to teach statistical and methodological concepts using surgical examples. Short versions of these courses were taught in Senegal during the 47th annual conference of the West African College of Surgeons in January 2007.

A full list of the projects that the CEU is currently undertaking can be found the College's website.

the Centre for Evidence in Transplantation

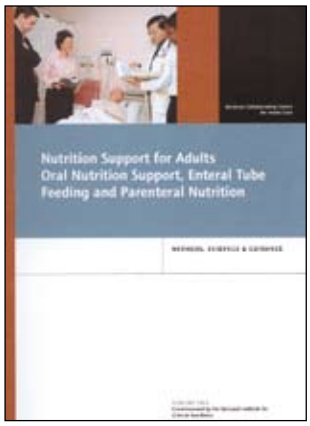
Professor Sir Peter Morris, Director

The past year has been a very productive one and has seen the staff grow from three to five. Two research fellows have joined the Centre for Evidence in Transplantation (CET), namely Neil Russell and Simon Knight from Cambridge and Oxford respectively, while Nishanthi Talawila has joined the team as both PA to the director and research assistant. Systematic reviews have been completed and published on Cyclosporine and C2 monitoring, the role of liver transplantation in hepatic malignancy and alemtuzamab in organ transplantation. The registry of randomised controlled trials continues to be published on a six-monthly basis by the journal *Transplantation*, but this is to be replaced by an electronic library of all randomised controlled trials back to 1970. The electronic library, which is very easy to search, will provide ready access to level one evidence for members of the transplantation community. This is to be launched in January 2008. Other projects include systematic reviews of calcineurin sparing or calcineurin-free immunosuppressive protocols in organ transplantation, a relook at mycophenolate mofetil and azathioprine and the value of monitoring of mycophenolate mofetil, a widely used drug in organ transplantation. The CET has reached an agreement with the European Society for Organ Transplantation to act as its knowledge centre, particularly with respect to helping to design and report randomised controlled trials within the European Community.

The National Collaborating Centre for Acute Care

Jennifer Hill, Director of NCC-AC

The National Collaborating Centre for Acute Care (NCC-AC) is funded by the National Institute for Health and Clinical Excellence (NICE) to produce evidence based clinical guidelines for the NHS.



The NCC-AC is now in its sixth year and this year has been one of intensive guideline development.

In February we proudly published our fifth national guideline, on nutrition support. This guideline helps the NHS identify patients who are malnourished or at risk of malnutrition and sets out the appropriate nutrition support that these people should receive.

The guideline recommends that:

- All hospitals inpatients on admissions and all outpatients at their first clinic appointment should be screened (weighed, measured and have body mass index (BMI) calculated). Screening should be repeated weekly for inpatients and when there is clinical concern for outpatients. People in care homes should be screened on admission and when there is clinical concern.
- Nutrition support should be considered in people who are malnourished, as defined by a BMI of less than 18.5; unintentional weight loss greater than 10% within the last 3–6 months; or a BMI of less than 20 and unintentional weight loss greater than 5% within the last 3–6 months.
- Nutrition support should be considered in people at risk of malnutrition, as defined by having eaten little or nothing for more than five days and/or being likely to eat little or nothing for the next five days or longer, who are unable to take in nutrients properly and/or who have increased nutritional needs.
- All acute hospital trusts should employ at least one specialist nutrition support nurse and establish a nutrition steering committee.
- All health care professionals who are directly involved in patient care should receive education and training, relevant to their post, on the importance of providing adequate nutrition.

Dr Mike Stroud of the Institute of Human Nutrition, University of Southampton and Chair of the Guideline Development Group says: ***"Ensuring patients receive adequate nutrition is an essential part of basic patient care, yet we know malnutrition is still a big problem for the NHS. The guideline contains one obvious and simple message: do not let your patients starve and when you offer them nutrition support, do so by the safest, simplest, most effective route. By recommending a widespread programme of screening and nutrition support, this guidance is likely to make a real difference and save lives."***

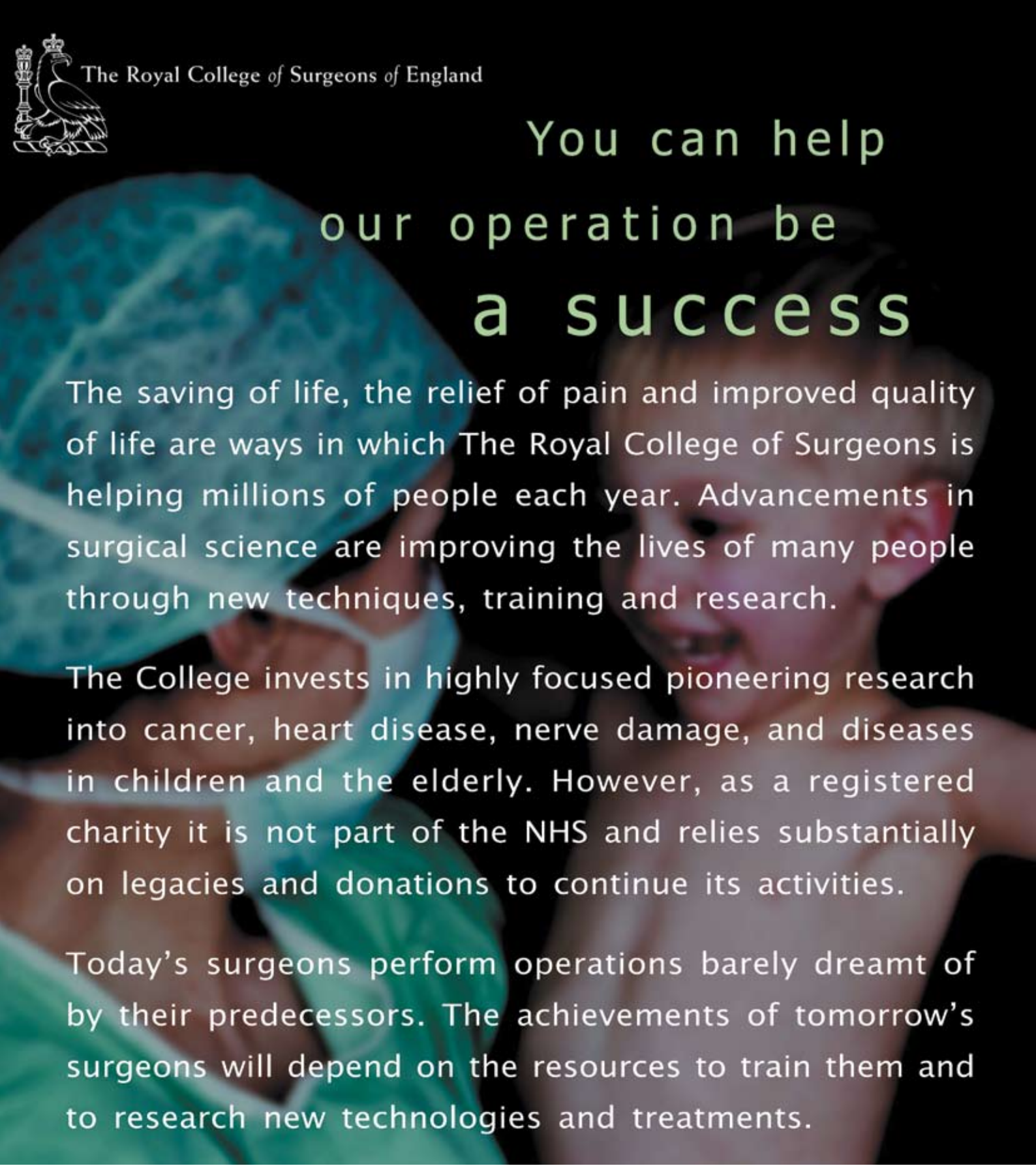
We have also been developing guidelines on reducing the risk of venous thromboembolism in surgical inpatients and the management of faecal incontinence. The NCC-AC worked with clinicians and patients to develop these guidelines and the first drafts for both guidelines have now been sent for stakeholder consultation. The venous thromboembolism guideline will be published in April 2007 and the faecal incontinence guideline will be published in June 2007. This year we are also updating our 2004 guideline on head injury, due for publication in September 2007.

This year the World Health Organisation conducted an independent review of the NICE guidelines programme. They identified as a strength the close links with the royal colleges and commended the work done to involve stakeholders and patients in developing the guidelines.

We are pleased to remain housed at the Royal College of Surgeons and continue to benefit from our close links with the Clinical Effectiveness Unit, the Centre for Evidence in Transplantation and the library.

We look forward to next year which should bring the launch of three of our guidelines and commencement of work on three new topics.

Summaries of all our guidelines are available to download from our website **www.rcseng.ac.uk/surgical_research_units/nccac/** or from NICE **www.nice.org.uk**. Printed copies of the full version of the guidelines, including details of all the research evidence, are available directly from the NCC-AC by email **ncc-ac@rcseng.ac.uk** or telephone **0207 869 6630**.



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