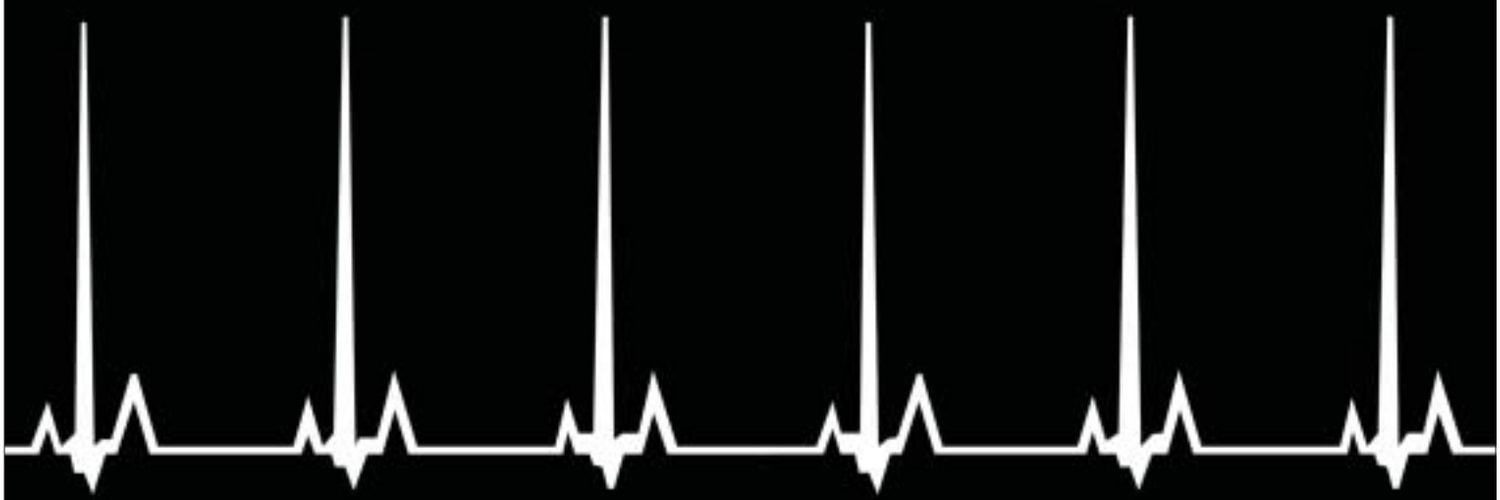
Research Report 2003/2004

CELEBRATING 10 YEARS OF THE RESEARCH FELLOWSHIP SCHEME

investing in research to improve patient welfare

Cazenove is pleased to support
The Royal College of Surgeons of England



CAZENOVE

12 Tokenhouse Yard London EC2R 7AN

CONTENTS

Introduction to Research Report 2003/2004

Professor Anthony Mundy

Director of the Research Department

Since Peter Bell wrote the introduction to last year's Research Report, several things have happened to him as some of you will know. Firstly, he has stepped down as Chairman and I have taken over from him. He and Martyn Coomer – who fortunately stays in post – have done such a wonderful job that it has been easy to step into his shoes. Secondly, he has been an industrious Vice-President of the College. Lastly, but by no means least, he received a knighthood in the Queen's Birthday Honours and I know you will all join me in congratulating him on this well-deserved honour and wish him well in his retirement from the University of Leicester.

This is the tenth anniversary of the Research Fellowship Scheme and we are marking the occasion with an all day event to celebrate the success of the last ten years to bring together those who have generously supported the scheme with those who have benefited from it; it is also an opportunity to plan for the future. We hope to do this jointly with the Society of Academic and Research Surgery (SARS) whose Secretariat has been relocated in the College alongside us. It is important to take stock of where we have got to with the **Research Fellowships** and the **Pump-priming grants** to be sure that we continue to do our very best to support research in surgery by making the best possible use of all available funds. We are, as always, very grateful to our existing and very loyal sponsors although it is disappointing that we do not have enough money for the many very good applications for research that we receive and therefore inevitably such good work does not get done because of shortage of funds.

We continue in particular to have strong support from the **Frances and Augustus Newman Foundation, The Enid Linder Foundation,** the **British Urological Foundation,** the **Dunhill Medical Trust** and the **Freemasons.** We have new sponsorship from the **Sir Jules Thorn Charitable Trust**, and we are delighted that the **Shears Trust** have agreed to renew funding of research in the north east.

This last year saw the first joint RCS/American College of Surgeons Fellowship. Miss Wai Yee Li, a young plastic surgeon, is spending two years in the Children's Hospital Los Angeles Research Institute as the first exchange with the American College of Surgeons. The past year also saw a further strengthening of our links with the Medical Research Council

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with whom we are trying to produce programmes to develop clinical scientists. These are relatively well developed in medicine but almost non-existent in surgery. We believe that the best way to develop surgical academics in the future is not simply to help them get an MD or a PhD but to allow them then to undertake post-doctoral or academic development alongside their clinical training. Therefore, there would not be the prolonged break between the MD and the academic aspirations.

We again tried to increase public awareness and raise money at the same time with a series of meetings in the College. In June 2002, we had an open afternoon for the public and an **'evening of presentations on surgical research'**. Subsequently, we had **'The New Genetics and Surgery'** and **'Waiting for Surgery'** meetings and have also held several *'Clinical Research Methods for Surgeons/Finding the Evidence*' courses ably organised by our academic colleagues in the Clinical Effectiveness Unit. All of these received excellent feedback and we shall continue to develop the programme of meetings into the future.

With all the changes in the College structure that have occurred in the last year, we are pleased to retain our close link with the **Clinical Effectiveness Unit**. They have a number of key projects described in detail later in this report and you will see that they continue to be invaluable for the College and for surgery in general.

As with most organisations, we go through periods of intense activity, particularly when it comes to assessing applications and deciding who is to be given one of the fellowships that we offer. This involves a large number of clinical, basic science and epidemiological assessors who rarely say no and willingly help with the assessment of these applications. Everybody works very hard in surgery these days and there is not enough time to do everything we need to. For assessors to take on this additional workload – usually at short notice and often involving considerable inconvenience and disruption – is probably the greatest single contribution to the effective running of the Research Department and I would like to express the department's gratitude for their efforts in the strongest possible terms.

Pictorial REVIEW of the year 2002–2003

2002

MAY02

Left: Jonathan Fountain, development director, addresses the Freemasons of Colchester and their spouses at a research evening.
Below: Mr David Rosin and research fellows in receipt of a cheque from the Somerset Freemasons following a research evening in Wincanton.

Right: Invitation to the bi-annual Research Evening held by the College.

JUNE02

Left: Pupils from Barrow Hills School, Surrey, enjoy participating in a workshop in the RCS Odontological Museum.

JULY02

Left: Sir Peter Bell steps down as chairman of the research board
Right: Miss Wai-Yee Li, research fellow, recipient of the first joint fellowship with the American College of Surgeons, with her supervisors at the Childrens Hospital Los Angeles. [From Left to Right: Tai-Lan Tuan, Professor David Warburton, Wai-Yee Li, Kathryn Anderson and Vesa Kaartinen]

AUGUST 02

Left: Posters advertising the Pump-priming grants and the research fellowships 2002/2003

SEPTEMBER 02

Left: The president with Bethan and Charlie Bennett-Lloyd before they embarked on an 8,000 mile cycle ride through South America, from Tierra del Fuego to the equator, to raise funds for a joint fellowship with The Stroke Association.

Above: Members of the Council enjoy a tour of the new Neath Hospital, hosted by Mr Russell Hopkins

OCTOBER 02

Above: Staff of the RCS shadowing Sir Peter Bell for the day as part of their Career Development Programme at Leicester Royal Infirmary.

Right: Poster advertising the Waiting for Surgery conference.

NOVEMBER 02

Left: Amjid Ali Riaz, the first European research fellow, being questioned by Professor Sir Peter Morris, as chief attacker, during his public viva for his PhD in Malmo, Sweden .

DECEMBER 02

Left: Research fellows and Faculty at the *Research Methods* course.

Far left: Professor Guy Maddern, Chairman of Research, Royal Australasian College of Surgeons in Adelaide.

2003

JANUARY03

Right: Christian Brown, Nicola Eardley and other research fellows at the diplomates ceremony.

Above: The mobile operating theatre parked at Warkworth Fire Station, New Zealand. This facility enables operations to be undertaken in isolated New Zealand communities.

FEBRUARY03

Above: Workshop given by Dr Jan van der Meulen, director of the CEU, at the *Research Methods* course.

Left: Mr and Mrs Shears with Mr Oparaku Umez-Eronini, The Northern research fellow.

MARCH03

Right: Steve Mannion and Sally Paul (far right) teaching on the College Hip Course, Blantyre, Malawi, generously supported by the Margossian family.

APRIL03

Left: Pallavi Mehrotra and Michael Kuo at the Otorhinolaryngology Research Society meeting at the Queen Elizabeth Hospital, Birmingham.

Right: Members of the Ethicon Travel Awards Committee reviewing applications.

MAY03

Left: Charles Collins, research fellows Nicola Smith and Nicola Eardley at a research evening for the Womens Institute kindly hosted by the Lady Mayoress of Hereford.
Below: Society of Academic and Research Surgery Council Meeting at the College.

JUNE03

Above: Bethan and Charlie Bennett-Lloyd cross the equator after cycling 8,000 miles through South America.

Above: Poster viva session in the RCS library to select research fellows for 2003.

JULY03

Left: Research fellows Evelyn Ong and Nigel Hall exhibiting at the British Association for Paediatric Surgery meeting in Estoril, Portugal.

AUGUST03

Left: President, Sir Peter Morris, and the vice-president, Miss Leela Kapila, on ward round at the Royal Darwin Hospital, Australia.

History of the Fellowship Scheme

There are few people who have not benefited in some way, either directly or indirectly, from advances made in surgical research. Research is the foundation of good surgical practice and forms an essential source of knowledge for the surgeon, the surgical profession and medicine as a whole. In the past, the College carried out its own in-house basic surgical research with significant results. However, major changes in research techniques led to concern about the viability of research away from a university or clinical environment. As a result of the College's review of its research activities in 1992, the Research Fellowship Scheme was created. 2003 marks the 10th anniversary of the College's Surgical Research Fellowship Scheme.

The Research Fellowship Scheme has the following objectives:

- **to contribute to improvements in patient care and recovery**
- **to assess new techniques introduced to surgery**
- **to look at the causes of surgical conditions and how to treat them**
- **to stimulate a commitment to life-long learning in surgical practice and technique, and understanding of research methodology.**

The Research Fellowship Scheme was set up to introduce a solid academic element into the clinical training of surgeons and to broaden their knowledge and experience. The aim is to ensure that future generations of patients will benefit from advances and improvements in surgical treatment and care, just as patients today benefit from research undertaken in the past. Only through surgical research will there come advances in surgical technique and management of surgical conditions. Each Fellowship endows a full-time research programme lasting from 1-3 years and which is supervised mainly in a UK department of surgery, but occasionally overseas. ***The Fellowships cover all surgical specialties, from neurosurgery to paediatric surgery; from transplantation biology to epidemiology. They cover a wide range of methods within surgical research, including basic science, anatomy, and physiology.*** A number of research projects are linked to innovative programmes, which are designed to resolve long-standing clinical problems. Some projects are self-contained, whilst others are part of a larger research programme.

We believe this is a powerful way of enhancing surgical research in this country and a development of national importance. It is a format that is now being duplicated by other institutions. ***Since the Scheme was launched in 1993, 301 research fellowships have been awarded throughout the country, totalling £11 million, and over the last 10 years the number and quality of applications has risen steadily, with over 100 applications received in the current round.***

Surgeons are asked to apply to the College each year with a detailed plan of the research they wish to undertake, supported in writing by the applicant's head of department and proposed research supervisor. All applications are rigorously assessed by a panel of internal and external experts, from all over the UK and abroad. These experts are independent of the candidate's hospital and university, and they ensure that the science, surgeon, supervision and facilities are of a high standard, and that the proposed work will be a valid, beneficial and original piece of research. They also check that the study design is thorough and that the work will be clinically relevant to patients. The assessors are aware of trends in certain illnesses and surgical techniques and can pinpoint the most appropriate research projects to fund. Once applications have been short-listed, candidates are invited to present a poster of their proposed work and be interviewed by a panel of senior surgeons before the final awards are made. These interviews are aimed at ascertaining the applicants' knowledge of the project and their role and aims in undertaking the research.

The College has an effective monitoring programme for each Fellowship and offers training and feedback sessions to the researchers. Additionally, the College is able to offer potential donors to the Research Fellowship Scheme authoritative knowledge of the best surgical research projects in a specialty, and can guide funding to almost any part of the country. This is why the College's role in the running of the Research Fellowship Scheme is so important.

In addition to the College's one year fellowships, the three-year research training fellowships, jointly funded by the Medical Research Council, have continued to be an outstanding success with awards made to two young surgeons each year. **Eight years ago the College also introduced Pump-priming grants to assist newly appointed consultants establish themselves in their chosen field of research – 58 of these grants were awarded.** These grants provided funds for pump-prime research studies, and are used to purchase equipment and secure technical support to strengthen the surgeon's research resources before they apply to larger programme grant funders. **The College also funds a limited number of international joint Fellowships, lectureships, travel and other awards.**

Approximately half the Fellowships have been funded through endowments and legacy funds left to the College by supporters, specifically for research. However, these funds are being depleted at an unsustainable rate, and we have to attract proportionately more external funding. Currently, charitable trusts, companies and individuals who recognise the value of surgical research **fund the other 50% of Fellowships through annual contributions. Each year the College aims to award between 20 and 30 fellowships, depending on the funds available.** The number of excellent applications we receive, however, has doubled since the scheme was introduced. ***We are currently unable to support 80% of those applying due to lack of funds***, and we are acutely aware that each year some highly-deserving applications go unsupported due to funding constraints. Our ability to make awards to the most deserving of cases is largely dependent on external sponsorship.

Securing funds to start a new research project is extremely difficult, and the College's one-year Research Fellowship Scheme has enabled researchers to collect the initial data and evidence necessary to apply to larger national funding bodies. Many of these new and innovative projects would not have been possible without this pump-priming.

Many fellows are also inspired to continue their research following a fellowship, thereby strengthening the College's academic base and providing the academic surgeons of the future.

Results from the research fellowships are disseminated widely through publications and presentations at national and international level, a number of which have in no small part contributed to greater understanding of diseases and have enhanced treatments for patients and improved surgical techniques.

Above left: Mr Eion Crighton who travelled by motorbike around the British Coastline, Spain, Portugal and the Sahara to raise funds for the Mary Crighton Stroke Research Fellowship. He continues to fundraise tirelessly on behalf of the RCS.

Above right: Marc Pacifico, research fellow, explaining his project to attendees at the Research Fellows evening, April 2003.

How charitable donations help fund the Research Fellowship Scheme

Some charitable donors to the Research Fellowship Scheme choose to support a complete piece of research each year, often linked to a specific illness or disease area, while others contribute to the scheme in general. Any amount donated to this important programme is greatly welcomed by the College, and allows us to expand the range and number of research projects we are able to support each year.

The College would be happy to discuss with potential donors how a donation could be directed to a specific surgical, geographical or disease area. Alternatively, we could provide a selection of high-quality applications from which the donor could choose.

Please write or call the Development Office at the College to discuss this further (direct telephone: 020 7869 6082).

Information on all the College's research funding opportunities can be found on the following website. **www.rcseng.ac.uk/surgical/research/**

Fellows who would like to find out more about how to apply for a College Fellowship can also obtain more information and an application form from the above web site.

If you are a fellow or member of The Royal College of Surgeons of England in a training post, or an SHO who has passed the MCQ papers and will sit the final MRCS (Eng) examination, you are eligible to apply.

We will support a number of one-year fellowships in any aspect of surgical care including basic science, diagnosis, treatment, surgical technology, logistics or audit. The fellowships cover salary, on costs and some running expenses.

Each fellowship is worth up to £45,000, which includes salary, National Insurance and other contributions, as well as an additional amount for consumables.

'Investing in research to improve patient welfare'

Profile of the College's Research Board
over the last 10 years

Before 1992, the College carried out its own in-house basic surgical research with significant results. The College's Hunterian Institute had a very distinguished record, including one Nobel prize and three Fellowships of the Royal Society.

However, major changes in research techniques, triggered especially by the advent of molecular biology, led to concern about the viability of research away from a university or clinical environment. As a result, the College undertook a comprehensive, external review of its research activities in 1992, under the chairmanship of Sir Michael Peckham. This review led to the decision by Council to reduce its support of research within the College and move some of the more active units to an appropriate medical school environment. Thus the biophysics unit was moved to the Institute of Child Health and the dental department was moved to the King's College School of Medicine and Dentistry; both units have profited enormously from the proximity of patients for their clinical research.

However, as the College remained committed to supporting research in surgery, the decision was made under the presidency of Professor Sir Norman Browse to attempt to do this throughout the UK by supporting, in the first instance, one-year research fellowships for surgical trainees with the eventual aim of supporting some fellowships for two or three years. **Thus, in 1992, the College's Research Fellowship Scheme and a more streamlined Research Board were created.**

The Research Board of the College exists to promote and fund surgical research throughout UK and worldwide, in all surgical specialties. Since 1992, the College has been fortunate in securing the support of three chairmen of research, whose wisdom, guidance and energies have contributed to the success of the College's surgical research programme.

Each chairman has made an important input into the development of surgical research in the UK, and has helped it gain respect and admiration

Left: Present and past chairman of the Research Board: (left to right) Professor Tony Mundy, Professor Sir Peter Morris and Professor Sir Peter Bell.

Professor Sir Peter Bell, recently retired head of surgery at Leicester, and formerly vice-president of the College, took over as chairman in 1997. He continued the work of his predecessor, especially in forging new, joint fellowships with other organisations and promoting the College's research overseas. Sir Peter also oversaw the establishment of the Clinical Effectiveness Unit (CEU), and the introduction of the *Research Methods Course* for recently appointed surgical research fellows. This course has proved invaluable in exchanging ideas and practices, and evaluating the Research Fellowship Scheme.

from many quarters. This is testified by the number of individuals, trusts and companies who support our research, and on whom the College, as a registered charity, depends heavily for funds to continue to advance surgery for the benefit of patients.

Professor Sir Peter Morris FRS, currently president of the College and formerly Nuffield Professor of Surgery at Oxford, was the first chairman of research under the new changes back in 1992. He steered the College's new research programme and department through the early years.

He established and consolidated the Research Fellowship Scheme, and worked to lay the strong foundations from which successive chairmen have benefited. Sir Peter's initial stewardship of the Research Department did much to raise the profile of both surgical research and the College amongst our fellows, and beyond.

The images on this page: Posters advertising some of the joint fellowships during the ten years of the research fellowship scheme.

Professor Tony Mundy, director of the Institute of Urology and Nephrology at University College London and Middlesex Hospital, and member of Council, is the current director of research. Having taken over in 2002, Professor Mundy is presiding over the 10th anniversary of the College's Research Fellowship Scheme. He plans to maintain the Research Department's excellent reputation in promoting surgical research by enhancing the role of the research committee, and evaluating the Research Fellowship Scheme. He is also keen to take forward research and development with the College's education programme.

Partnerships

The College is fortunate to have secured the support of many partners, who share our commitment to advance standards in surgery and combat surgical illnesses. The future of surgical research depends on the availability of research funds and we are very grateful to all those individuals and organisations who have contributed to the Research Fellowship Scheme over the last 10 years, and whose valued interest in surgical research is demonstrated by their regular attendance at College events such as the surgical research evenings.

The support we receive from many of our fellows is also deeply appreciated and we would like to encourage more fellows to consider donating regularly via gift aid. This will ensure that surgeons of the future continue to benefit from the research fellowship scheme. For further details about donations, telephone the Development Office on 020 7869 6082.

We are pleased to have received the following endorsements from three of our current funders. We hope that they will inspire others to support surgical research through the Research Fellowship Scheme.

THE DUNHILL MEDICAL TRUST

'The Dunhill Medical Trust is pleased to be able to make a difference to the advancement of surgery through its support of the Research Fellowship Scheme of The Royal College of Surgeons. We know that these fellowships achieve real results for patients.'

The Dunhill Medical Trust

The Dunhill Medical Trust has supported the College's research programme for over 35 years. This support has assisted the College in funding high quality research projects from a wide range of surgical specialties, which it may not have otherwise been able to fund. The Trust is currently supporting a two-year research fellowship in Liverpool. Nicola Eardley is investigating new gene therapies for pancreatic cancer, and it is hoped this research will lead to more effective treatment for this distressing disease, which kills some 7,000 people in the UK each year.

THE FOYLE FOUNDATION

'The Foyle Foundation supported the College for the first time this year. We were impressed by the quality and potential impact of the research, which the research fellow is undertaking, and by the College's strict peer-review process that all applications undergo before being submitted to charitable organisations for funding.'

The Foyle Foundation

As bowel cancer accounts for the second highest number of cancer death in the UK, the Foundation is jointly funding a one-year research fellowship to enable Charles Bailey to continue his research to identify inflammatory factors in bowel cancer called chemokines. These contribute to cancer growth. The aim is to develop new therapies to block the action of the chemokines, and improve survival.

CANCER RESEARCH UK

'Cancer Research UK is delighted to be able to support two high quality surgical research fellowships. We believe that these projects will yield valuable and important results in the understanding and treatment of cancer.'

Cancer Research UK

Cancer Research UK is currently co-funding two research fellowships, in London and Sheffield. These projects aim to increase understanding of prostate cancer and to enhance the treatment of bladder cancer – two common cancers about which we know very little.

The college would like to offer its particular thanks to the following:

Foundations, charitable trusts and corporate donations

Britannic Assurance plc

BUPA

Caedmon Lodge Freemasons

Masonic Lodge of Science

Angel Lodge Freemasons

The Lodge of Hope Freemasons

The Cazenove Charitable Trust

The Andrew Anderson Trust

The Bernard Sunley Charitable Foundation

The Caravan Club (Suffolk Centre)

The Charles and Elsie Sykes Trust

The Dunhill Medical Trust

The Enid Linder Foundation

The Family Rich Charities Trust

The Fitton Trust

The Frances and Augustus Newman Foundation

The George Drexler Foundation

The T R Golden Charitable Trust

The Grand Lodge of Freemasons 250th Anniversary Fund

The Jeff Waterside Cancer Research Fund

The Joseph Strong Frazer Trust

The Kirby Laing Foundation

The Lady Stevens Fellowship

The Shears Charitable Trust

The Thomas Sivewright Catto Charitable Settlement

The Vandervell Foundation

The Wyndham Charitable Trust

Joint awards

British Association of Plastic Surgeons

British Association of Paediatric Surgeons

British Association of Endocrine Surgeons

British Urological Foundation

British Vascular Foundation

British Association for Surgery of the Knee

Cancer Research UK

RAFT (Restoration of Appearance and Function Trust)

Society of Academic and Research Surgery (SARS)

The Healing Foundation

The Ileostomy and Internal Pouch Support Group

The American College of Surgeons

The Medical Research Council

The Botnar Family,

The British Society for Surgery of the Hand

WOMAC

Endowments and legacy funds

The Andersen Reid Fund
The Bernhard Baron Fund
The Harold Bridges Bequest
The Buckston Browne Gift
The Burghard Bequest
The Burton Legacy
The Norman Capener Fund
The Campbell Legacy
Children with Cancer
The Lillian May Coleman Fund
The Collett Legacy
The Harry Morton Exchange Fund
The Margossian Bequest
The Stefan Galeski Bequest
Darlow Research Fellowship
The M E Davis Fund
Denker Legacy for Research in the UK
The Ellin Legacy
The Fellows Fellowship Fund
The Fletcher Legacy
The B L Herbert Funds
The Hiller Legacy
The Sydney Jacobs Fellowship
The Kanaar Legacy
The Kennard Legacy
The Laming Evans Fund
The Sir John Lang Legacy
The Edward Lumley Fund
The Lea Thomas Funds
The Harry Morton Fund
The Moser Fund
The Muirhead Legacy
The Osman Hill Collection and Research
The Parks Visitorship
The Mrs. J. M. Phillips Legacy
The Preiskel Family Fund
The Prophit Trust
The Joan Robb legacy
The Shortland Legacy
The Simpson Legacy
The Sir Arthur Sims Fund
The Tudor Edwards Fellowship
The Vandervell Research Fund
The Watts Legacy
The Kate Weeks Fund

Left: H.R.H the Duke of Kent being admitted as an honorary fellow of the College.

His Royal Highness the Duke of Kent is admitted as an honorary fellow

In February 2003, His Royal Highness the Duke of Kent, as Grand Master of the United Grand Lodge of Freemasonry, was admitted as an honorary fellow of The Royal College of Surgeons of England. This was in recognition of the charitable support given by English Freemasonry to the College's surgical research programme. Through his association with Freemasonry, His Royal Highness has been actively involved in supporting many health-related charities and organisations including the College. The Royal College of Surgeons has a long and special relationship with Freemasonry in England with the advancement of surgery owing much to the generosity and constant support of Freemasons, who have contributed money and time to the College and its Surgical Research Fellowship Scheme over many years.

Research Fellows Evening – June 2002

The Research Fellows Evening for College supporters and sponsors was held in June last year, and was introduced by the College president, Professor Sir Peter Morris and chairman of the Research Board, Professor Sir Peter Bell. Fellows presenting their research included Miss Rachel Kimber, Enid Linder Research Fellow; Mr Marcus Bisson, RAFT/Kirby Laing Research Fellow; Miss Claire Taylor, Joint RCS/St Peter's Trust Research Fellow; and Mr Ajay Kakkar, Pump-priming grant recipient. The evening was attended by 65 supporters and has now become an established and popular annual event. Guests particularly enjoyed the question and answer session following the presentations, which was followed by an opportunity to meet the researchers and other surgeons at an informal reception.

Research Fellows Evening – April 2003

Another successful research evening was held in April this year. Again, the evening was introduced by the College president, Professor Sir Peter Morris, together with the new director of research, Professor Tony Mundy. Around 80 guests listened to presentations by Mr Alex Thornton-Smith, The Lady Stevens research fellow; Miss Pallavi Mehrotra, Royal College of Surgeons fellow sponsored by the Shears Charitable Trust and the British Association of Endocrine Surgeons; Mr Andrew Davies, BUPA fellow; and Miss Nicola Smith, Royal College of Surgeons research fellow with support from the T R Golden Charitable Trust.

Past Research Fellows

Mr Simon Kenny

Simon Kenny was awarded the Fellows Research Fellowship in 1996/1997 for a project entitled 'The role of endothelin 3 and its receptor in the aetiology of Hirschsprung's disease'.

Mr Kenny says of the fellowship scheme:

'Babies born with Hirschsprung's disease lack nerve cells in the large bowel and present shortly after birth with life–threatening bowel obstruction. My work led to six publications in peer-reviewed journals and I obtained

my MD in 2000. More importantly, in association with David Lloyd (professor of paediatric surgery) and David Edgar (senior lecturer in human anatomy and cell biology) we have been able to obtain funding for three further research fellows, two of whom to date have obtained MD degrees with ongoing publications in the field. To date we have been supported by the generous assistance of Action Research; the Digestive Diseases Foundation; Pilkingtons Charitable Foundation; SPARKS; the Children's Nationwide Research Foundation; the Birth Defects Foundation and further research fellowships from The Royal College of Surgeons of England to Mark Woodward (who won the Patey Prize in 1999) and Emma Sidebotham (BAPS prize 2001). Currently we are studying the basic behaviour of the stem cells that 'seed' the bowel to create a nervous system in the gut during the development. This holds the potential for understanding many gut-motility related diseases in addition to potential new treatment for children with Hirschsprung's disease. The Research Fellowship Scheme has been the backbone that has supported us in the early years as we have established a track record that allows us to effectively compete for funding – thank you!'

Mr Christopher Wigfield

Christopher Wigfield was awarded the Catherine Cookson Trust Research Fellowship in 2000/2001 for a project entitled 'Amelioration of Donor Injury after Brain Death in Lung Transplantation'

Mr Wigfield says of the scheme:

'The Royal College of Surgeons Research Fellowship Scheme has provided numerous trainee surgeons with outstanding academic opportunities. More importantly, it has meant effective progress in various fields of surgical research. Project funding and methodological assistance have often relied on investigators' ingenuity. The Research Fellowship Scheme has actually created a new standard of excellence by providing both in a dedicated program.

Personally, the rewards have been immense. Significant further funding was secured for a PhD fellow project to employ my research model, confirming its value. To complete a meaningful scientific study has demonstrated my commitment in my chosen career path. It definitely inspired me to approach clinical problems with a more systematic and reflective attitude as a specialist registrar in cardiothoracic surgery.'

Mr Philip Roberts

Philip Roberts was awarded the Laming Evans Research Fellowship in 1997/1998 for a project entitled 'Hip fractures in older people'.

Mr Roberts says of the fellowship scheme:
'There are two value aspects in being awarded a College research fellowship. The first is the benefit in pure science advance that is important but the second, that perhaps I could concentrate upon, is how this period is able to shape and give direction to your career development.

Your period of fellowship allows acquisition of new skills, essential tools for the researcher but not always so strong in the clinician. Training courses in word-processing, graphic design, poster publication, statistics, critical appraisal, public speaking and database establishment all spring to mind as very basics. In later projects and exams all these skills, however, become welcome secondary skills.

The research ethos that you gain during your fellowship arms you with better insight about starting or becoming involved with later projects and gives you more of a bench mark about which ones are likely to be successful and hence worth your time investment, an important lesson to carry through registrar training.

My personal development has been significantly boosted by this training because of the new insight and skills provided. I was fortunate to go on to become a trainee on the Oswestry/Stoke Orthopaedic Scheme, in no small part to the kudos provided by being the Laming Evans Fellow. I passed the FRCS (Orth and Trauma), helped by my wider armamentaria gained during the fellowship, and have been appointed consultant orthopaedic surgeon with perhaps 20% of my appointments committee interview being a discussion about my College-based research.

Miss Lorna Marson

Above: Miss Lorna Marson (2nd from right) with (left to right) Katie Grace, Magdi Shehata and Jared Torkington at a surgical workshop, Sindh Institute of Urology Transplantation, Karachi.

Lorna Marson was awarded the Dunhill Medical Trust Research Fellowship in 1996/1997 for a project entitled 'Angiogenesis: its role in breast cancer and the effect of tamoxifen treatment'. She was awarded her MD in 1999 from the University of Edinburgh.

Miss Marson says of the fellowship scheme:
'The research fellowship provided an opportunity for me to undertake laboratory research, of which I had no previous experience. Having completed the project I maintained an interest in research during my clinical training and have been awarded grants to fund technical and research staff. The opportunity provided for me by the fellowship led me to decide to pursue a career in academic surgery. In January 2003 I was awarded a Clinician Scientist Fellowship by the Academy of Medical Sciences and Health Foundation to investigate the role of macrophages and angiogenesis in the development of chronic rejection in renal transplantation at the University of Edinburgh.

The Research Fellowship Scheme not only provided me with this fabulous opportunity to undertake research but also offered a network of support during my research and an opening into the College of which I am a fellow.'

Research Reports

PUBLICATIONS

The European Journal of Surgical Oncology and the *British Journal of Surgery*.

PRESENTATIONS

The 7th Nottingham International Breast Cancer Conference.
The Europoean Society of Surgical Oncology, April 2002.
The Association of Surgeons of Great Britain & Ireland Annual Meeting, 2002.
The Annual Scientific Meeting of the British Association of Surgical Oncology, 2002.

NAME

Amanda L Thorne

TITLE OF STUDY

Increasing the detection of metastases in patients with breast cancer using mammaglobin as a marker

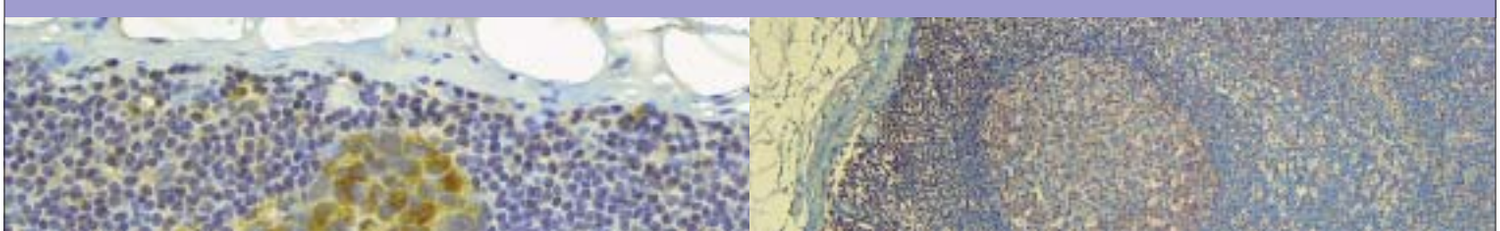
SITES OF WORK
Breast Unit, Queen Alexandra Hospital, Portsmouth and University of Portsmouth

FELLOWSHIP/SPONSOR
Dunhill Medical Trust

FURTHER FUNDING
Portsmouth Hospital NHS Trust

SUPERVISORS
Professor Mike Perry, professor of surgery, Queen Alexandra Hospital, Portsmouth

Professor Colin Crane-Robinson, professor of biological sciences, University of Portsmouth



Above, left and right: slides showing axillary lymph nodes from a patient with breast cancer. Immunohistochemical staining using the mammaglobin antibody shows the metastases in a brown colour.

15–20% of breast cancer patients, who although they have early breast cancer and negative axillary lymph nodes, go on to have recurrence of the disease. They may experience pain and limitation of their normal day-to-day activities, or require further surgery, chemotherapy and radiotherapy treatments.

If we can accurately identify breast cancer patients who are at risk of a recurrence, then preventative treatments can be given. A great deal of work has been undertaken to improve the detection of breast cancer metastases (cancer cells that have spread from the original tumour) and this study aims to further extend our ability to detect this spread.

Mammaglobin is a protein produced in breast tissue and is over-produced by breast cancers. As mammaglobin is not expressed outside the breast its presence in other tissues indicates that breast cancer cells have spread from the original tumour.

A group of 30 out of 101 patients were found to have mammoglobin expression in histologically negative lymph nodes. This may represent patients where lymph node metastases have been missed by standard investigations.

I will collect data during the clinical follow-up of patients which will give us important survival and disease recurrence information and enable us to determine the true benefit of using mammaglobin expression to predict patient outcome in breast cancer.

I was inspired to undertake this work by the previous Dunhill research fellow. My work was a natural progression from the research fellow who preceded me and another is now moving on from where I left off.

PUBLICATIONS

The Journal of Urology 1999 **162:**1833–1839.

The Journal of Urology 2001 **166:**1530–1533.

Neuropharmacology 1997 **36:**1127–1139.

Right: Professor Burnstock and Freddie Banks reference searching through Professor Burnstock's vast reference libraries.

NAME

Freddie Banks

TITLE OF STUDY

Purinergic signalling in the obstructed bladder

SITE OF WORK
Royal Free Hospital, London

FELLOWSHIP/SPONSOR
Special Trustees of the Royal Free Hospital

SUPERVISORS
Mr Robert Morgan, consultant urologist

Professor Geoffrey Burnstock, director of the Autonomic Neuroscience Institute, University College London

Urinary incontinence represents a massive clinical problem. It is estimated that over two million suffer from some form of incontinence within the UK. Bladder outflow obstruction, as occurs with an enlarging prostate, can lead to the bladder muscle becoming 'unstable'. It is this bladder instability that is thought to be the cause of incontinence in approximately one third of women sufferers, and half of men.

The mainstay of current treatment for bladder instability is with anticholinergic medication. This is at best effective in only 70% of those treated, and side effects cause at least a quarter of those to stop treatment. Recent studies have suggested that bladder instability may be caused by muscle contractions due to neurally-released ATP (purinergic signalling). Treatment of the abnormal ATP component could potentially offer a different, or synergistic line of treatment. This study examined rat bladder contractions in a model of bladder obstruction. The model aimed to mimic the pathology that occurs in the ageing male that develops with an enlarging prostate. It was hoped to uncover the mechanisms involved in the development of ATP-induced bladder contractions.

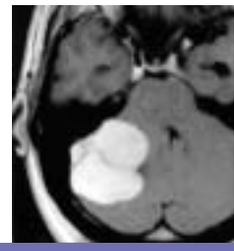
Bladder instability causes severe physical and social disability, and the impact on people's lives is hugely underestimated. I have been very disappointed with the current pharmacological treatment for bladder frequency and it was this disappointment that inspired me to undertake this project.

The research builds on 35 years of work by Professor Burnstock, and more immediately of my predecessor Rob Calvert into purinergic signalling. It is hoped further research will be conducted into the obstructed, or unstable bladder, as well as the role of purinergic signalling in other urological disease states.

I have learnt a great deal about the techniques of scientific research, statistics, the evaluation of papers and scientific writing. This knowledge has been hugely beneficial to me in my understanding of both scientific and clinical papers. If surgeons are to practice evidence-based medicine, then a period in research is essential for a true understanding of scientific methodology. The development of this project, with particular reference to establishing a successful partial bladder obstruction model, was hugely satisfying.

PRIZES

The Norman Dott Medal 2002 from the Intercollegiate Board in Neurosurgery.



NAME

Andrew Martin

TITLE OF STUDY

Mechanisms of local invasion by meningiomas

SITE OF WORK
Institute of Psychiatry, University of London

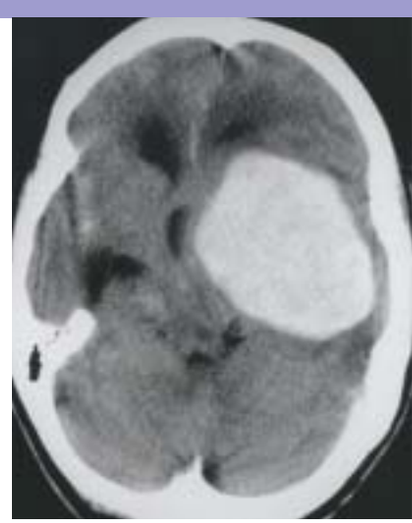
FELLOWSHIP/SPONSOR
The Grand Lodge of Freemasons 250th Anniversary Fund

SUPERVISORS
Professor GJ Pilkington, professor of experimental neuro-oncology

Dr HK Rooprai, senior lecturer in experimental neuro-oncology

Meningiomas are the second most common intracranial tumour and treatment generally involves surgery. Although most meningiomas are benign, many show invasion of the dura mater, skull and, more rarely, the brain itself. There is a significant long-term recurrence rate even after apparently complete excision and, in many cases, total removal is difficult as the tumour has grown around critical nerves and vessels. Therefore, local invasion is a significant problem in the management of meningiomas and our aim was to investigate this behaviour.

The study comprised three main areas. We aimed to develop more realistic models of tumour behaviour as tumour cells grown in the laboratory often have significantly different properties to those found in living tissue. We also used tissue staining techniques to investigate brain invasion by meningiomas. Finally, with colleagues at the University of East Anglia, we studied the levels of matrix metalloproteinases (MMP) found in meningioma cultures – MMP are strongly implicated in the ability of tumour cells to migrate through tissues.



Once this study has been completed I hope that our improved understanding of meningioma biology will lead to better patient care. I was an SpR in neurosurgery in South Thames, recently spent one year as SpR and skull base fellow at the Wessex Neurological Centre and have now been appointed as a consultant at the Atkinson Morley Wing, St. George's Hospital, London. I hope that our experience with new cell culture techniques will continue to be used for the study of meningiomas and other intracranial tumours.

"There is a significant long-term recurrence rate of meningiomas even after apparently complete excision."

PUBLICATIONS

Prostate Cancer and *Prostatic Diseases*.

PRESENTATIONS

Annual Congress of the European Association of Urology, Geneva. April 2001.
Annual Conference of the British Association of Urological Surgeons, Dublin. June 2001.
The British Prostate Group Autumn Meeting, London. Sept 2001.
Third International Conference on Cancer-induced Bone Disease, Awasi, Japan, Nov 2001.
European Association of Urology Annual Congress, Madrid. March 2003.

NAME

Ben Thomas

TITLE OF STUDY

The role of bone morphogenetic protein-6 (BMP-6) in the formation of skeletal metastases in prostate cancer

SITE OF WORK
Academic Urology Unit,
University of Sheffield

FELLOWSHIP/SPONSOR
Bernard Black Memorial Fellowship

SUPERVISORS
Professor FC Hamdy, professor of urology
Dr NJ Brown, reader in surgical sciences

In the advanced stages, prostate cancer spreads to bone, which can cause pain, fractures and, at worst, paralysis. How and why this occurs remains poorly understood. BMP-6 has been previously implicated and solving this puzzle could help to prevent the spread of this cancer.

In conjunction with colleagues at Newcastle-upon-Tyne University, human prostate cancer cells were genetically altered so that they produced increased amounts of BMP-6. The effect on growth and spread of the cancer was determined by injecting mice with modified and unaltered cells.

The results show that increased levels of BMP-6 cause prostatic tumours to grow more rapdidly and these tumours cause symptoms at an earlier stage in the disease process. However, numbers of metastases are not increased.

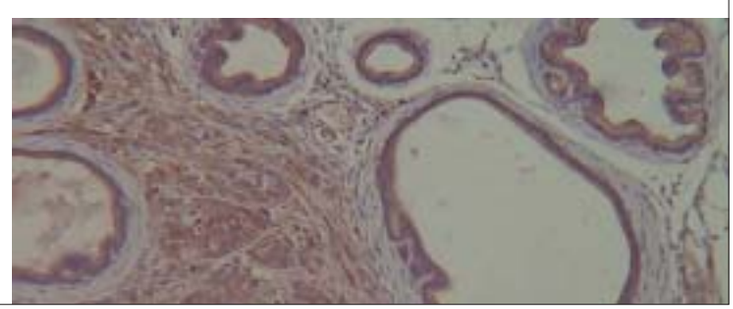
Current treatment options for metastatic prostate cancer are limited. Any potential new therapeutic agents could significantly improve quality of life, or in an ideal world, prevent metastasis altogether.

The experimental approach that I established, which included some aspects that were introduced for the first time in the UK, is now being used for other research projects, and depending on the final outcome of my work it may well be taken further.

"BMP-6 appears to accelerate the growth of prostatic tumours."

I would recommend undertaking a period of research because it is not an area that we are widely exposed to during surgical training. A good understanding of research methodologies and processes is increasingly important because surgeons with these skills are more able to evaluate published research and determine how it can be used to improve patient care. By giving trainees this opportunity, research can help to nurture future academic surgeons.

Below: Immunohistochemical staining for BMP-6 in a prostate tumour. The brown areas represent cells containing the protein. At the top of the picture normal prostate tissue is seen, with tumour invading from the bottom of the image.



PUBLICATIONS

Surgery 2003; **21(6)**:141–143.
BJU International 2003; **92(1)**:53–57.
BJU International 2003; **91(1)**:30–33
European Association of Urology guidelines on Benign Prostatic Hyperplasia, 2002

PRIZES

£150,000 BUPA Foundation research grant.

PRESENTATIONS

BAUS, 2002 and 2003.
British Prostate Group, 2002 and 2003.
World Congress of Urology 2003.

NAME

Christian Brown

PROJECT TITLE

Self-management for men with uncomplicated lower urinary tract symptoms

SITES OF WORK

Clinical Effectiveness Unit (CEU), The Royal College of Surgeons of England and Institute of Urology and Nephrology, University College London

FELLOWSHIP/SPONSOR

Cazenove & Co.

FURTHER FUNDING

BUPA Foundation

SUPERVISORS

Mr Mark Emberton, CEU deputy director and senior lecturer and consultant urological surgeon, University College London

Dr Jan van der Meulen, CEU director

Professor Anthony Mundy, professor of urology, Institute of Urology and Nephrology, University College London

Above: Recruiting a patient into a clinical trial.

Lower urinary tract symptoms affect 70% of all men over the age of 65. Self-management in those with uncomplicated symptoms has never previously been investigated.

Lower urinary tract symptoms, including passing urine more frequently and urgently and occasional incontinence, can cause embarrassment and can interfere with daily life, leading some men to restrict their activities. This study assesses how effective self-management of lower urinary tract symptoms can lead to improvements in symptoms and quality of life for affected men, without the need for drugs or surgery.

We have successfully developed and tested a programme of self-management for men with uncomplicated lower urinary tract symptoms. Twenty-five men have so far participated in the programme and, through nurse-led self-management sessions, have leant new skills and behaviours to allow them to manage their symptoms themselves. The three main components: education and reassurance, lifestyle modification, and behavioural interventions, have been shown to be effective in the short term reduction of symptoms. All the men have experienced an improvement in their quality of life and a reduction in urinary frequency which has been associated with an increase in the volume of urine passed.

I would recommend research to any surgeon. I felt very proud to be involved in the project from the beginning, taking it from an idea to a well received and effective clinical intervention. I intend to complete my MD at the University of London and am seeking an SpR post in the capital. I would like to continue with an academic interest in urology.

"70% of all men over the age of 65 have lower urinary tract symptoms ... self-management can dramatically improve their quality of life."

PUBLICATIONS

Surgery 2002; **132(6)**:998–1007.

PRIZES

BJS best paper prize, British Association of Endocrine Surgeons 2002.

PRESENTATIONS

Society of Academic and Research Surgery (SARS) Dublin and London, 2002.
American Association of Endocrine Surgeons 2002. Banff Springs, Canada, 2002.
British Association of Endocrine Surgeons. Pisa, Italy, 2002.
The 102 Annual Congress of Japan Surgical Society, Kyoto, Japan 2002.

NAME

Chris Wong

TITLE OF STUDY

The role of insulin-like growth factor system and Wilms tumour suppressor 1 gene in hyperparathyroid disease

SITE OF WORK
Division of Surgery, University of Bristol

FELLOWSHIP/SPONSOR
Louis Alexander Surgical Research Fellowship

FURTHER FUNDING
Mason's Medical Research Foundation
Hamamelis Trust
Royal Society
Lord Dowding Fund for Humane Research

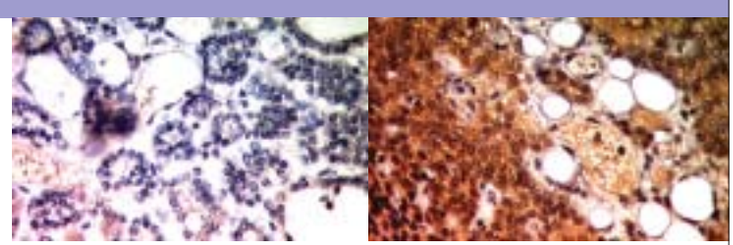
SUPERVISORS
The late Professor JR Farndon, professor of surgery
Professor MH Wheeler, professor of surgery

The parathyroid gland helps to regulate the amount of calcium in the blood and in hyperparathyroidism the balance is disrupted and blood calcium rises. This produces a range of symptoms including weakness and fatigue with more severe symptoms such as nausea, vomiting, constipation and confusion.

We studied how Wilms tumour suppressor 1 gene expression differs in normal and hyperparathyroid specimens. We also examined the role of insulin-like growth factors in the pathogenesis of hyperparathyroidism.

Using parathyroid cell cultures we investigated the insulin-like growth factor system in a live environment. The effects of various potential therapeutic agents was also investigated.

This study determined that Wilms tumour suppressor 1 gene expression is reduced in hyperparathyroid tissue. The reduction in suppressor activity is associated with increased levels of insulin-like growth factors I and II which increase parathyroid cell growth.



Above left: Immunochemistry of insulin-like growth factor 1 receptor of a normal parathyroid gland showing little staining.
Above right: Immunohistochemistry of Wilms tumour suppressor 1 gene of the same specimen showing nuclear staining of the gene product.

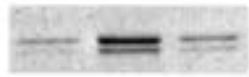
This study further determined that both retinoic acid (a vitamin A derivative) and tamoxifen inhibited such growth.

Presently, surgery is the only definitive treatment for hyperparathyroidism. As a result of our research we have started a clinical trial where patients suffering from primary hyperparathyroidism will receive a course of vitamin A supplement or placebo. The preliminary results are encouraging.

I am proud to have developed this project from its embryonic stage into a piece of work worthy of a PhD. I am hoping to complete further specialist training in the form of a fellowship in the UK or abroad before applying for a consultant post. This period of research has enabled me to approach clinical problems with much more clarity and helped me to develop much better problem solving plans. Most of all, research has empowered me to 'question'.

PUBLICATION

The Journal of Pediatric Surgery.



Above: Western blotting demonstrates significant differences in protein expression.

NAME

Emma Parkinson

TITLE OF STUDY

Intestinal ischaemia-reperfusion: investigating the mechanisms of hypothermic protection

SITE OF WORK

Institute of Child Health, University College London.

FELLOWSHIP/SPONSOR

Harold Bridges

FURTHER FUNDING

Children's Research Fund

SUPERVISORS

Professor Agostino Pierro, professor of paediatric surgery

Dr Simon Eaton, non-clinical senior lecturer

Gastrointestinal diseases characterised by intestinal ischaemia-reperfusion can occur in newborn babies, children and adults and are important causes of morbidity and mortality. Ischaemia-reperfusion injury arises when blood flow is temporarily stopped (ischaemia) and then restarted (reperfusion). Early protective actions could prevent subsequent multiple organ failure and reduce the need for extensive surgery in patients with intestinal ischaemia-reperfusion injury.

Whole-body moderate hypothermia can protect against the multiorgan effects of intestinal ischaemia-reperfusion. I aim ultimately to replicate its protective effect without modulating temperature.

To investigate the potential beneficial effects of moderate hypothermia in an animal model, ischaemia-reperfusion damage to the gut was induced. The animals were maintained at either normal temperature (36–37°C) or moderate hypothermia (30–33°C). I then examined gut, liver and lung extracts to determine whether hypothermic protection is mediated by changes in the expression of proteins important in preserving cell function.

> "I feel proud to have discovered something previously unknown and to have opened a window for further research in this field."

Preliminary results support the potential therapeutic role of moderate hypothermia in regulating cell death and preventing organ dysfunction. This finding may lead to the identification of new therapeutic targets in patients with conditions characterised by intestinal ischaemia-reperfusion.

I plan to complete my PhD at the Institute of Child Health and am currently looking for an SpR post while continuing to work for the Children's Research Fund. I would definitely recommend research as it is an opportunity to step back from a busy clinical environment and develop a new understanding of a disease and new approaches to its treatment.

PRIZES

Lund University Research Fellowship, PhD University of Lund.

PUBLICATIONS

Annals of Surgery 2002; **236:**777–84.
British Journal of Surgery 2002; **89(12):**1572–80.
British Journal of Pharmacology 2002; **135(7):**1749–56.

PRESENTATIONS

Brish Association of Coloproctology, Manchester, UK July 2002.
European Society of Surgical Research, Szeged, Hungary. May 2002.
European Surgical Association, Lisbon, Portugal, April 2002.
Asian Society Transplantation, New Delhi, India, Feb/March 2002.
British Association of Plastic Surgery, Nov 2001.

NAME
Amjid Ali Riaz

TITLE OF STUDY

Ischaemia/reperfusion induced leukocyte-endothelial interactions in the colon

SITE OF WORK
Department of Surgery,
Malmo University Hospital,
Lund University, Sweden

FELLOWSHIP/SPONSOR
European Surgical Research Fellowship

FURTHER FUNDING
Lund University Research Fellowship

PROJECT SUPERVISORS
Professor Bengt Jeppsson, professor of surgery
Dr Henrik Thorlacius, associate professor

Ischaemia/reperfusion (I/R) damage is common in surgery and is significantly associated with morbidity, mortality and organ dysfunction. I/R damage occurs when blood flow into tissue is stopped and then restarted. This is important in transplantation, trauma, vascular and GI surgery. Our aim was to study the destructive role of white blood cells in the colon after induction of I/R.

This is a totally new and exciting project with very little published work on the subject. The project has been expanded and many researchers are taking forward the results of our unique findings.

After inducing I/R in the colon of a mouse, there was a significant increase in the number of rolling and firmly adherent white blood cells. The effect was mediated by oxygen free radicals (OFRs) and drugs that reduced OFRs ameliorated this response. We further explored the role of adhesion molecules on this process namely P-selectin and the beta-2 integrin LFA–1. Protective effects of Heparin and Fragmin in I/R-induced tissue injury were also discovered. My findings were very well received.

If we are successful, the quality of life for surgical patients will eventually be improved. All branches of surgery may potentially benefit from the reduction of pathological inflammation after ischaemia/reperfusion injury.

I intend to complete my specialist registrar training and would like to set up my own research group with the help of my own grant. I thoroughly recommend research to other surgeons. It is exciting and fun no matter what the results. Pursuing research means developing your knowledge of another aspect of surgery and improving your opportunities for future surgical practice. It can also help with reading and assessing published data, statistics and setting up clinical research.

Left: Amjid in the laboratory examining histopathologhy slides using a light microscope.

"This is a totally new and exciting project with very little published work on the subject ... many researchers are taking forward the results of our unique findings."

PUBLICATIONS

Eur J Vasc Endovasc Surg 2002; **24(6):**505–510.
Eur J Vasc Endovasc Surg 2002; **23(3):**209–211.
Br J Surg 2001; **188(12):**1590–1594.

PRESENTATIONS

Surgical Research Society, 2000.
Vascular Surgical Society of Great Britain and Ireland, 2000 and 2001.
European Society of Vascular Surgeons, 2001.

NAME

Ganeshamoorthy Kuhan

TITLE OF STUDY

The application of mathematical modelling techniques for risk adjustment and comparative audit of carotid surgery

SITE OF WORK
Hull and East Yorkshire NHS Trust

FELLOWSHIP/SPONSOR
The Grand Lodge of Freemasons 250th Anniversary Fund

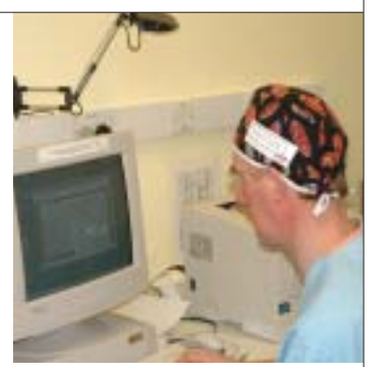
SUPERVISOR
Professor PT McCollum, professor of vascular surgery, Academic Vascular Unit, University of Hull

"Risk adjustment and comparative audit can help to define national standards of patient care."

Patients who have carotid disease are at a high risk of stroke and other cardiovascular complications. Carotid endarterectomy (CEA) is a surgical procedure which reduces the risk of stroke. In our study, a history of stroke, heart disease and diabetes increases the risk of a further stroke or death following CEA by five times. One in ten diabetics who undergo CEA have a stroke or die within thirty days of the procedure.

The purpose of my study was to develop risk models to compare surgeons' performances and to predict the risk to patients. Risk adjustment and comparative audit aim to improve clinical effectiveness and can help to define national standards of patient care.

The use of new mathematical models in risk prediction greatly fascinates me as their application in medicine is at an early stage. Also, there is a great need to develop risk models which will aid in comparative audit. I was therefore proud to win the research fellowship, which helped to establish the Academic Vascular Unit in East Yorkshire. I would recommend research to budding surgeons as it is an investment for the future. Current clinical practice will not remain static and changes will be made through evidence-based medicine.



Above: Peter McCollum entering data as soon after an operation. Who, when and where data is collected is crucial for data quality.

I am currently a clinical fellow in the Academic Surgical Unit, Castle Hill Hospital, Hull and I intend to complete my MD at the University of Hull.

PRIZE

First prize for best paper presented at Canadian Society of Surgical Oncology Annual Scientific Meeting 2002.

PRESENTATIONS

British Academic Conference in Otolaryngology 2003.

The Sixth Research Workshop on the Biology, Prevention and Treatment of Head and Neck Cancer 2002.

American Academy of Otolaryngology-Head and Neck Surgery Foundation Annual Meeting 2002.

NAME

Giles Warner

TITLE OF STUDY

Molecular classification of oral squamous cell carcinoma using cDNA microarray analysis

SITE OF WORK

The Wharton Head and Neck Unit, Princess Margaret Hospital, Toronto

FELLOWSHIP/SPONSOR

The Harry Morton Travel Research Fellowship

SUPERVISORS

Professor Suzanne Kamel-Reid, Princess Margaret Hospital, Toronto

Professor Bryan Young, Cancer Research UK, Medical Oncology Unit, St Bartholomews Hospital Medical School.

The Harry Morton Traveling Research Fellowship is a joint venture between the Canadian and English Royal College of Surgeons to encourage surgeons to perform research outside their own country.

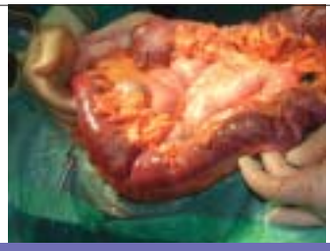
I spent one year as a research fellow at the Wharton Head and Neck Cancer Unit – part of the Ontario Cancer Institute, a tertiary referral center for head and neck oncology – based at the Princess Margaret Hospital, Toronto. The allied laboratory is the main Canadian basic sciences center for head and neck cancer and has a huge bank of fresh frozen and paraffin-embedded specimens for molecular research.

Head and neck cancer is the sixth most common cancer with just under half a million new cases per year worldwide. Despite improvement in loco-regional control, the combined treatment options of surgery, radiation and chemotherapy has not improved the overall survival of these patients, and 50% die within five years. There is therefore much interest in the molecular biology of these tumors with the aim of improving diagnosis, therapeutic decisions and prognosis.

Left: Classification of 20 oral cancers based on the similarity of gene expression profiles. Each map represents the gene expression profile of a single tumor. The colors represent clusters of differentially expressed genes. Thus cancers with similar expression profiles are grouped together. Group 1 and 2 correlated with size and nodal status of the tumor and overall were a better predictor of disease free survival than conventional outcome predictors.

This project involved using a novel genetics tool called microarray analysis to identify gene expression profiles in oral squamous cell carcinoma. Microarray analysis identifies the expression of thousands of genes simultaneously, thus providing a 'snapshot' of the genetic activity of the tumor. These 'snapshots' are known as gene expression profiles. Expression profiles were identified that correlated with both nodal metastasis and tumor size in oral cancer. Moreover, classification of the tumors based on their expression profile was a better predictor of disease free survival than conventional outcome predictors. These and other findings from microarray analysis may have important implications in the staging of tumors and may ultimately lead to improvement in clinical decisions resulting in a better prognosis for these patients.

"Classification of the tumors based on their expression profile was a better predictor of disease-free survival than conventional outcome predictors."



PRESENTATIONS

British Society of Gastroenterology (BSG) Glasgow 2001.
Association of Coloproctology of Great Britain & Ireland (ACPGBI), Harrogate 2001.
International Society for Analytical Cytometry (ISAC), Montpellier 2000.

NAME

Ian Bradford

TITLE OF STUDY

Regulation of Neutrophil Chemotaxis in ulcerative colitis

SITE OF WORK
Department of surgery, University of Newcastle.

FELLOWSHIP/SPONSOR
Ileostomy Association and Internal Support Pouch Group

SUPERVISOR
Mr Stefan Plusa, consultant colorectal surgeon

Above: Extensive colitis showing discoloured and inflamed colon in the foreground.
Below: Toxic dilatation of the colon with imminent perforation due to severe ulcerative colitis.

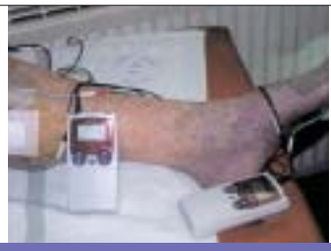
Ulcerative colitis is a disease characterised by abnormal inflammation of the colon. Interference with the normal immune process allows pathogenic organisms and pro-inflammatory substances to enter the gut which then promote and perpetuate the damage. We examined the role played by one such group of substances, the chemokine family, in affected patients.

Biopsies from normal and inflamed colon were analysed by a technique called immunohistochemistry to detect molecules called CXCRs, which act as the 'gatekeepers' of the inflammatory process driven by chemokines. We then developed a laboratory model of the chemokine process of inflammation. This allowed us to study the effects of individual chemokines and the CXCRs in both diseased and healthy tissue. The influence of antibodies to block these substances was assessed as a potential therapy for ulcerative colitis.

Chemokines were detected on several populations of white blood cells, most notably the polymorphs. These cells could be induced by bacteria and their products to create the chemokines, as is believed to occur in ulcerative colitis. When colonic inflammation was extensive, the chemokines were detected in the circulation as well, suggesting a contribution to systemic upset seen in such cases. Using the laboratory model, we have been able to quantify the effect of each chemokine and to show the potential to block its effects through CXCRs. We have now documented the presence of CXCRs on circulating white blood cells, the cells lining the capillaries and within the colon lining. All sites are thus potential therapeutic targets.

Most interestingly, colon biopsies from ulcerative colitis patients showed increased levels of CXCRs, regardless of whether the colon appeared inflamed or whether patients were symptomatic. This suggests that this disease may in part be due to a constitutional abnormality of CXCRs.

"Interestingly, colon biopsies from ulcerative colitis patients showed increased levels of CXCRs, regardless of whether the colon appeared inflamed or whether patients were symptomatic."



PRIZES

Winner, best poster presentation, arterial section, European Microcirculation Society, 2002.
Winner, best presentation, cardiovascular session, Leicestershire Research Day 2002.

PRESENTATIONS

Basic science section at the Vascular Surgical Society of Great Britain and Ireland, 2002.
The British Association of Plastic Surgeons, 2001.
The European Microcirculation Society, 2002.

NAME

James Clover

Above: Patients were initially randomised into treatment and control groups. The treatment group applied two TENS stimulators, for three one hour periods each day for a six week period.

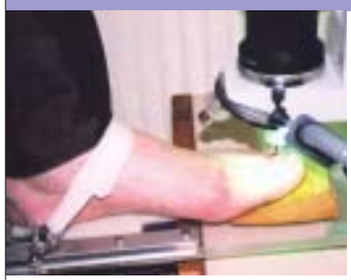
TITLE OF STUDY

A potential non-invasive method for the stimulation of therapeutic angiogenesis

SITE OF WORK
Department of Surgery, University of Leicester

FELLOWSHIP/SPONSOR
Frances and Augustus Newman Foundation Fellowship

SUPERVISORS
Dr NPJ Brindle, lecturer in cell biology
Mr MJ McCarthy, lecturer in surgery



Left: Photograph showing the foot of a patient positioned for capillary microscopy. Capillaries are illuminated in the skin and can be visualised and quantified. An increase in capillary density was seen after six weeks of subcontractile electrical stimulation when assessed by this method. This increase in capillary density was confirmed on muscle biopsies.

Intermittent cramping pain, the need for peripheral arterial reconstruction, or at worst, amputation, can all affect patients with peripheral vascular disease. In fact, amputation rates are rising in patients with the disease despite an aggressive limb-salvage policy.

This study aimed to search for a non-invasive method for inducing new blood vessel growth in situations where there is inadequate blood supply. This could potentially have far-reaching benefits: from treatment of patients with peripheral vascular disease to wound healing and tissue transfer.

Initially , laboratory based research showed that sub-contractile electrical stimulation could induce release of vascular endothelial growth factor (VEGF), which is involved in blood vessel growth. A subsequent clinical trial recruited patients with peripheral vascular disease. Sub-contractile electrical stimulation was administered to areas of skeletal muscle in each patient to determine its effect on the density of blood vessels.

Patients were assessed for changes in transcutaneous oxygen tension and capillary density in their skin and muscle before, during and after a six-week treatment period.

Sub-contractile electrical stimulation at the optimum frequency (8Hz, 10mA) increased capillary density and transcutaneous oxygen tension in a localised area in patients with peripheral vascular disease. This non-invasive method of increasing capillary growth in tissues with poor blood flow could have great clinical potential.

It is anticipated that others will continue to develop this as a potential treatment for patients with peripheral vascular disease. I also hope to explore the use of this type of stimulation in the healing of cutaneous ulcers and in tissue transfer.

I have enjoyed making a contribution to scientific knowledge, and as such, would recommend research to any surgeon.

PRIZES

Otto Zennestrom prize for the best paper at the 2002 European Hyperbaric Association Meeting.

PRESENTATIONS

Undesea and Hyperbaric Medicine Association 2002.
European Hyperbaric Medicine Association, 2002.
Tripartite Colorectal Meeting, 2002.

NAME

Jeremy Cundall

TITLE OF STUDY

Treatment of faecal incontinence secondary to pudendal neuropathy with hyperbaric oxygen

SITE OF WORK
Academic Surgical Unit, Castle Hill Hospital, University of Hull

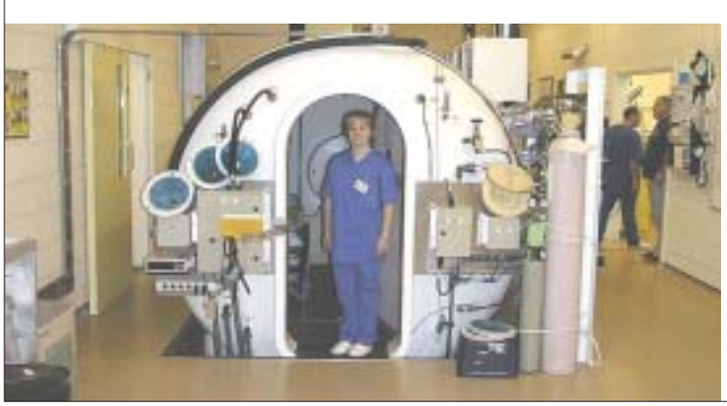
FELLOWSHIP/SPONSOR
Simpson

SUPERVISOR
Mr GS Duthie, reader in general surgery

Faecal incontinence, which is obviously extremely distressing, is sometimes caused by nerve damage (neuropathy) to the pudendal nerve. This nerve supplies the muscles of the anus.

The aim of this project was to see if treatment with hyperbaric oxygen (oxygen at pressures greater than normal atmospheric pressure) could improve the function of the pudendal nerve in patients with faecal incontinence secondary to chronic neuropathy. If nerve function could be improved then it was hoped that patients' faecal incontinence could also be helped.

We studied patients who had faecal incontinence for two years or more who also had damaged pudendal nerves. They received thirty hyperbaric oxygen treatments over six weeks. Nerve function was tested sequentially throughout the treatment and also one and six months after the treatment had finished. Patients also filled in questionnaires on their incontinence and quality of life.



We found a statistically significant improvement in the pudendal nerve, which was maintained at six-month follow up. Although two-thirds of patients said their symptoms had improved, we found that their quality of life had not changed significantly, which indicates how distressing these symptoms can be.

I wanted to find a treatment for the cause of faecal incontinence with the worst prognosis, ie pudendal neuropathy. The study has produced some excellent clinical data which will be carried on into further trials. The long-term aim is to establish a multicentre randomised controlled trial comparing biofeedback to hyperbaric oxygen for these patients.

I am currently doing an SpR rotation in general surgery in the Northern Deanery.

Left: A multiplace Hyperbaric chamber.

PRESENTATION

Induction of Insulin-like Growth Factor Binding Protein-3 by Hypoxia and Increased Urinary Excretion in Bladder Cancer. J.J.Ord E.Streeter D.Cranston A.L.Harris. British Cancer Research Meeting. August 2003

NAME

Jonathan Ord

TITLE OF STUDY

Analysis of pathways involved in bladder cancer invasion and metastasis

SITE OF WORK
Churchill Hospital Oxford

FELLOWSHIP/SPONSOR
The George Drexler Foundation

FURTHER FUNDING
Oxford Health Services Research Committee

SUPERVISORS
Professor Adrian Harris, professor of medical oncology, University of Oxford

Mr D Cranston, consultant urologist

Fifty per cent of patients with invasive (malignant) bladder cancer die within five years of diagnosis despite major surgery or radiotherapy.

Unlike normal human tissue bladder cancers, like many other solid cancers, have areas in them that are very low in oxygen (hypoxia). The cancer cells that are able to survive hypoxia are known to activate a group of genes such as VEGF that have been shown to be related to the growth and spread of invasive bladder cancer.

Two such genes, HIF and VEGF, have been shown to be of key importance and the therapeutic value of drugs against these genes is being researched by others. Areas of low oxygen in tumours are also known to be resistant to radiotherapy which is a mainstay of bladder cancer treatment.
We wanted to look for other unknown genes that might be activated in areas of low oxygen.

We wanted to find new pathways that may also be markers to detect cancer or targets for therapy. We found that 52 genes from a study of 10,000 were significantly upregulated by a low oxygen environment. Some of these genes were known, like VEGF but others were novel. One such gene, IGFBP3 was found to be significantly raised in the urine of patients with invasive bladder cancer and may be important for survival of the cancer cells.

Left: Graphic representation of hypoxia inducible genes (rows) in 39 bladder tumours (columns). Some genes are turned on in all tumours (red rows) othersappear turned off (green rows). The most clearly upregulated genes are IGFBP3 and VEGF. IGFBP3 has not been investigated in relation to bladder cancer before and is a potential therapeutic target of the future.

We also aim to ascertain whether the level of hypoxia in a tumour is an independent predictor of prognosis. An initial study of 73 bladder cancers suggests this maybe true for invasive cancers. This initial finding is now being further investigated.

"Unlike normal human tissue, bladder cancers are very low in oxygen which results in activation of pathways causing aggressive growth."

PUBLICATIONS

Cerebrovascular Diseases 2002; **13(suppl 4):**6 (O19).
Heart; **88(suppl iv):**iv29.
Cerebrovascular Diseases 2003; **16(suppl 2):**1–2, 6, 17.
European Surgical Research 2003; **35:**183–184.

PRESENTATIONS

The 7th European Neurosonology and Cerebral Haemodynamics Meeting, Berne, Switzerland, May 2002.
The British Hip Society, Belfast, February 2003.
The European Society for Surgical Research, Ghent, Belgium, May 2003.
The 8th European Neurosonology and Cerebral Haemodynamics Meeting, Alicante, Spain, May 2003.

NAME
Kevin Daly

TITLE OF STUDY

The role of paradoxical emboli in major surgery

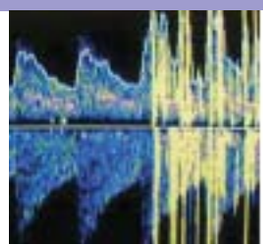
LOCATION OF WORK
South Manchester University Hospital

FELLOWSHIP/SPONSOR
The Three Peaks Trust

FURTHER FUNDING
Manchester Surgical Research Trust

SUPERVISOR
Professor McCollum, professor of surgery, University of Manchester

About one in five healthy people have a defect in their heart called a patent foramen ovale. This is the most common defect allowing blood to flow directly from the veins to the arteries bypassing the filtering effect of the lungs.



Above: Transcranial Doppler ultrasound detection of microscopic bubbles in the brain confirming the presence of a patent foramen ovale.

We found that particles released during hip and knee operations passed to the brain only in people with this circulation defect. As patients frequently suffer confusion and organ damage following major surgery, I wanted to investigate whether the damage caused by these particles could be a prevented cause of damage to vital body organs.

Particles released during hip replacement surgery were detected in the brain circulation in 58% of patients, and the number of particles was closely related to the size of the circulation defect. However, the number of particles had no influence on brain, heart, kidney or liver function.

Additional research performed during this fellowship showed an ultrasound test for a heart defect was a reliable and reproducible method of identifying patients at risk of organ damage from particles released during surgery. A study of patients with a fractured hip showed that particles in the brain circulation were common following the fracture and during surgery. These particles were associated with deterioration in brain function, particularly in memory.

I really enjoyed my research fellowship. The project offered a real and exciting opportunity to study a potentially reversible cause of complications following surgery. I'm now skilled in the use of Doppler ultrasound and have an understanding of research methodology skills that are readily transferable to my surgical training. After I have completed the fellowship and my MD, I'll join the North West Region general surgery SpR rotation. I hope to return to clinical training and continue to use the skills that I have learnt during this period for future research studies.

"Fat particles are commonly found in the brain circulation during hip surgery"

PUBLICATIONS

Clinical Otolaryngology and Allied Sciences.

PRESENTATIONS

South and West Laryngological Association, Cardiff.
Otorhinological Research Society, Manchester, March 2002.

NAME

Claire Langton Hewer

TITLE OF STUDY

Development of the eighth nerve ganglion in the mouse and the role of transcription factors NeuroD and GATA3

SITE OF WORK
Department of Physiology, School of Medical Sciences, University of Bristol

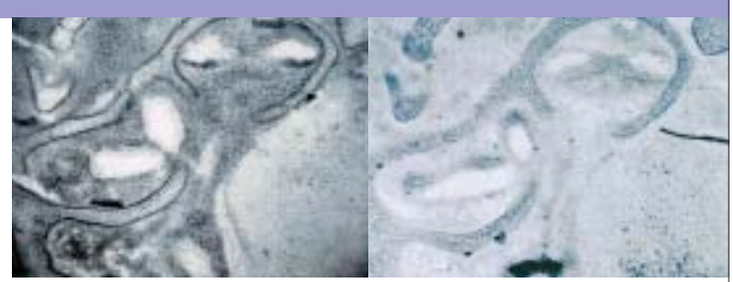
FELLOWSHIP/SPONSOR
Burghard Fellowship

SUPERVISOR
Professor Matthew C Holley, Institute of Molecular Physiology, University of Sheffield

Deafness affects 10% of the world's population and can be a very isolating condition because of its impact on our ability to communicate with each other.

Nerve deafness is currently incurable. Conventional hearing aids are of some help but there remain many limitations, particularly in making them sufficiently frequency-selective. The ultimate goal of this study is to produce 'immortal' nerve cells in an injectable form. These could be injected into people with nerve deafness and would develop sufficiently to make connections with other parts of the brain. This type of treatment would revolutionise our current management of hearing loss and abrogate the need for hearing aids.

We studied the development of auditory nerve cells in mouse embryos and identified two transcription factors that were critically important; NeuroD and GATA3. Transcription factors are proteins which alter the function of genes. We found that both these factors were expressed in the early embryonic stages of cells which would become auditory nerves. These inner ear cells are programmed to develop along a specific path depending upon which protein is present. This information will help us to program immortal cells in the future.



Above left: GATA label of whole ear at embryonic day 15. **right:** NeuroD label of whole ear at embryonic day 15.

It was an honour to be part of an internationally recognised research group. I was proud to see the first draft of our paper and will be even more delighted when it is finally printed. Scientific research is a challenging discipline which requires endless patience and optimism. The literature can be very inaccessible in the early stages but understanding proceeds with time. Determination and persistence are necessary through the difficult times when experiments fail.

"Deafness can be a very isolating condition because of its impact on our ability to communicate with each other."

PRIZES

Phillip Stell Prize. Otolaryngology Research Society. Hull, 2001.
First Resident Award. The 4th European Laryngology Society Meeting, Brussels, 2002.
John A. Garner Prize. The Yorkshire Regional Otolaryngology Research Meeting. Leeds, 2002.

PUBLICATIONS

International Journal of Cancer 2002; **100:**472–475.
British Journal of Cancer 2003; **89**: 864-869.

PRESENTATIONS

The British Association of Surgical Oncology Annual Meeting. Glasgow, November 2001.
Autumn meeting of the Otolaryngology Research Society. London, September 2002.
The 4th European Laryngology Society Meeting, Brussels, September 2002.

NAME

Luke Condon

TITLE OF STUDY

The role of chromosome 22 in the progression of head and neck cancer

SITE OF WORK
University of Hull, Division of Cell and Molecular Medicine, Castle Hill Hospital.

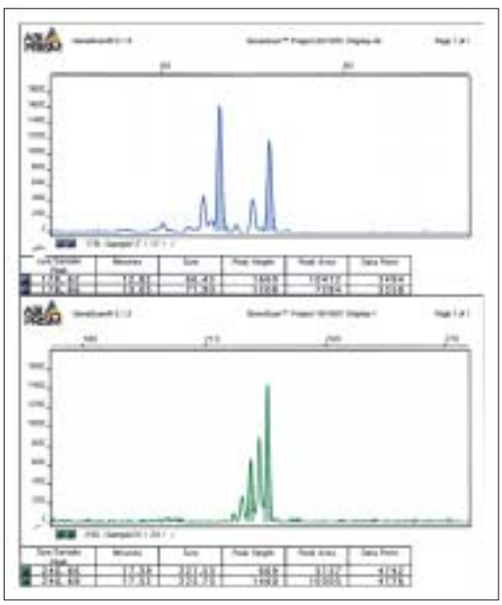
FELLOWSHIP/SPONSOR
The Grand Lodge of Freemasons 250th Anniversary Fund

FURTHER FUNDING
Head and Neck Research and Development Fund, Hull Royal Infirmary

SUPERVISORS
Dr Lynn Cawkwell, lecturer in genetics, University of Hull

Dr John Greenman, senior lecturer in surgery, University of Hull

Professor Nick Stafford, professor of otolaryngology, head and neck surgery, Hull Royal Infirmary



Left: Typical electrophoretograms of a heterozygous (blue peaks) and a homozygous (green peaks) sample of DNA.

Cancer of the head and neck region, for example the tongue or voice box, has a tendency to spread to the lymph glands in the neck. Fewer than 50% of patients with lymph node metastases at the time of diagnosis will survive beyond five years. Increasing our understanding of the mechanisms of cancer spread will clearly help us to develop new cancer treatments.

Preliminary work in our laboratory suggested that abnormalities of chromosome 22 may be important in enabling cancer cells to spread to the lymph glands in the neck. We used genetic probes and a sequencing machine to compare the chromosome 22 status of normal, cancer and metastatic cells in patients with head and neck cancer.

Our findings suggest that there is little difference in chromosome 22 between normal cells and cancer cells, but that there may be an abnormality of chromosome 22 in cancer cells that have successfully spread to the glands in the neck. One particular area of genetic alteration on chromosome 22, encodes an enzyme called MMP-11. We performed further studies, using immunohistochemistry, that confirmed the presence of higher levels of MMP-11 in cancer cells that had spread. This enzyme is able to digest connective tissue, and so may play a role in allowing cancer cells to leave the site of the primary tumour and spread to the lymph glands.

This work could help in the development of new treatments and preventative strategies for metastatic neck disease, which may significantly improve patient survival. After completing my specialist registrar rotation, I would like to obtain a consultant post that will allow me to maintain my interest in academic surgery.

PUBLICATIONS

Journal of Hand Surgery (British and European Volume) 2003 **28(4):** 351–356.

PRESENTATIONS

European Conference of Scientists and Plastic Surgeons. Helsinki, September 2001.
British Society for Surgery of the Hand Autumn Meeting, London, October 2001.
Summer British Association of Plastic Surgeons meeting, July 2002.
European Conference of Scientists and Plastic Surgeons, Vienna, September 2002.
British Society for Surgery of the Hand Autumn Meeting, Edinburgh, November 2002.

NAME

Marcus Anthony Bisson

TITLE OF STUDY

The contractile properties of cells derived from Dupuytren's disease

SITES OF WORK

The Raft Institute of Plastic Surgery, Mount Vernon Hospital and TREC (Tissue Repair and Engineering Centre), The Institute of Orthopaedics, Royal National Orthopaedic Hospital

FELLOWSHIP/SPONSOR

RAFT/The Kirby Laing Foundation Research Fellowship 2001/02

FURTHER FUNDING

The British Society for Surgery of the Hand

SUPERVISOR

Mr Adriaan O Grobbelaar, consultant plastic and reconstructive surgeon

Dupuytren's disease affects 1 in 10 men over the age of 65. As disease progresses tissue shortens, preventing patients from extending their fingers. Recurrence occurs following surgery for the disease in up to 60% of patients. The condition can prevent continuation of pastimes or occupations. Even simple activities of daily living can become embarrassingly difficult.

Dupuytren's disease has two clinical forms, nodules and cords. We hypothesised that nodule derived fibroblasts have differing properties to those from cord. Additionally, Dupuytren's disease cells may have inherently altered contractile properties. By understanding these characteristics we may be better placed to halt development of progressive flexion deformities.

Nodule and cord cells were cultured and stained to show the percentage of contractile myofibroblast cells in each type of cell culture. Then a culture force monitor was used to determine the force produced by each cell type as they contracted collagen gel samples.

We discovered that Dupuytren's cells can be reactivated by growth factors possibly leading to recurrence.

Dupuytren's cells display abnormal contractile properties and responses to applied tension. This could be crucial in understanding why contractures develop.

I am proud to have been involved in a high quality research project in a well-respected unit that has yielded exciting and new results. From this I have been able to present my work at national and international meetings and have already submitted two research papers based on the studies. Meanwhile, my thesis has been submitted, and I have successfully secured an SpR post in plastic surgery.

Below: Setting up an experiment using Dupuytren's disease fibroblasts on the culture force monitor.

NAME

Paris Tekkis

TITLE OF STUDY

Risk adjustment in gastrointestinal surgery

PUBLICATIONS

British Medical Journal 2003; 326, 986-8
British Journal of Surgery 2203; **90**:340-5.
ACPGBI Colorectal Cancer Study 2002. Part B: The ACPGBI Colorectal Cancer Model.
Association of Coloproctology of Great Britain and Ireland, June 2003

PRIZES

Hunterian Professorship 2002/2003.
British Journal of Surgery Prize for Best Oral Presentation at the Association of Upper GI Surgeons of Great Britain and Ireland Scientific Meeting, Edinburgh 2001.

PRESENTATIONS

The Tripartite Meeting, Melbourne, 2002.
Association of Coloproctology of Great Britain and Ireland Annual Meeting, Manchester, 2002.
The American Society of Colon and Rectal Surgeons Annual Convention, Chicago, 2002.
Association of Surgeon of Great Britain and Ireland Annual Meeting, Dublin, 2002.

SITES OF WORK

King's College Hospital, London

St George's Hospital, London

FURTHER FUNDING

NHS Information Authority

FELLOWSHIP/SPONSOR

Huey Falwasser Research Fellowship

SUPERVISORS

Professor IS Benjamin, professor of surgery

Dr Jan Poloniecki, senior lecturer in biostatistics

One in fourteen patients with colorectal cancer die within thirty days of surgery and one in eleven patients with stomach and oesophageal cancer die during their initial in-hospital stay.

A total of 33,000 new patients are diagnosed with bowel cancer in the UK every year, of which 90% undergo surgery. The success of surgery can vary depending on how far the disease has progressed at the point when a patient goes into hospital. It is therefore important to establish the best method of treatment through an objective method for evaluating risk and outcomes of such patients. The aim of the project was to develop prediction models for providing risk estimates for individual patients undergoing bowel and stomach cancer surgery. Artificial intelligence systems and conventional statistical models were used for comparing surgical performance between hospitals and for monitoring the quality of health care within units.

New oesophagogastric and colorectal statistical models were developed and were shown to have better performance than the existing systems.

Artificial neural networks were better at individualising risk than their statistical counterparts in upper gastro-intestinal surgery. Mortality control charts were found to provide an accurate, risk adjusted means of identifying units at the extremes of the population while providing early warning signals of divergence from the national average mortality.

Above: Mr Paris Tekkis and Dr Jan Poloniecki at St George's Hospital.

The project formed a landmark for future research in surgical outcomes, it has expanded to national and international levels and is currently being supported by the Association of Coloproctology of Great Britain and Ireland, the NHS Information Authority and the Cleveland Clinic Foundation, USA.

PUBLICATION

Prescriber 2002; **13 (9):**47–57.

PRIZES

The Royal Society of Medicine Laryngology and Rhinology Section Equipment Grant Award, 2002.

Left: Rami with his supervisor Dr Peter Howarth in the image analysis unit

PRESENTATION

Proceedings of the Autumn Meeting of the Otolaryngological Research Society, London 2002.

NAME

Rami J Salib

TITLE OF STUDY

Mechanisms of epithelial activation and mast cell chemotaxis in allergic rhinitis

SITE OF WORK

Department of Respiratory Cell and Molecular Biology, Division of Infection, Inflammation and Repair, Southampton General Hospital.

FELLOWSHIP/SPONSOR

The Louis Alexander Fellowship

FURTHER FUNDING

Frances and Augustus Newman Foundation Two-year Fellowship

SUPERVISORS

Dr Peter Howarth, reader in medicine and honorary consultant physician

Dr Susan Wilson, senior research fellow and head of the histochemistry research unit, University of Southampton

Left: : Immunohistochemical staining of TGF-beta 2 and TGF-beta receptor 2 in glycol methacrylate-embedded sections of nasal mucosa from subjects with seasonal (in season) and perennial rhinitis, showing enhanced immunoreactivity levels in the nasal epithelium (brown staining).

Allergic rhinitis represents a global health problem affecting between 10% and 25% of the world population. Even more worryingly, the prevalence of the condition has been increasing steadily over the past 10 years. The impact of the disease is often under-appreciated with afflicted patients having a significantly impaired quality of life. Furthermore, the disease has a profound socio-economic impact with direct medical costs, and considerable indirect costs relating both to absences from work and school, and reduced productivity. An analysis of the indirect and direct health care costs related to allergic rhinitis within the USA identified an annual economic burden in excess of $3.0 billion.

Currently, the treatments available (antihistamines and corticosteroids) suppress the symptoms but do not tackle the cause of the disease. One of the main cells involved in allergy is the mast cell and this study was designed to learn more about how mast cells migrate into the nose and thus cause symptoms in individualswith rhinitis.

Using immunohistochemical methods, we compared reactive cells from tissue samples from the nasal lining of healthy controls, symptomatic grass pollen related hay fever sufferers (seasonal rhinitis) and in people suffering with house dust mite sensitivity (perennial rhinitis). We also performed immunological staining for various chemical substances and receptors.

I wish to extend my preliminary findings to test the hypothesis that, in persistent allergic rhinitic subjects, the nasal epithelium is more susceptible to injury leading to an altered epithelial phenotype associated with enhanced production of proinflammatory mediators that sustain persistent inflammation. With funding secured for the next two years, I hope that I will be able to complete a PhD.

"Allergic rhinitis has a profound socio-economic impact with direct medical costs, and considerable indirect costs relating both to absences from work and school, and reduced productivity."

PUBLICATION

Journal of Paediatric Surgery 2003; **38 (1):**37–44.

PRIZE

Winner of the Peter Paul Rickham Prize at the 2002 British Association of Paediatric Surgeons Conference.

PRESENTATIONS

The European Society for Parenteral and Enteral Nutrition, Glasgow 2002.
BAUS Cambridge 2002.
BAUS Estoril, Portugal 2003.

NAME

Robin Garrett-Cox

TITLE OF STUDY

Glutamine, a novel therapeutic agent in neonatal sepsis?

SITE OF WORK
Department of Paediatric Surgery, Institute of Child Health

FELLOWSHIP/SPONSOR
The Grand Lodge of Freemasons 250th Anniversary Fund

SUPERVISORS
Professor Agostino Pierro, professor of paediatric surgery
Dr Simon Eaton, non-clinical senior lecturer

1–5% of live births have an episode of sepsis (a severe illness caused by infection in the blood) in the neonatal period which is associated with a 10–15% risk of mortality.

My aims were to assess the outcome of glutamine administration in newborn babies with sepsis, and to study its role in reducing the effect of infection on the baby's metabolism. If successful, this work could help to reduce the length of stay in neonatal intensive care units and help to reduce the mortality associated with infections in the neonatal period.

By looking at various factors in the blood of infected rat pups and their overall metabolism, I could determine whether there was any marked improvement in those that had been given glutmamine. Infected newborns can end up with an energy failure and reduced oxygen consumption as the rat pups become sick. Glutamine injections partially restored this reduced oxygen consumption. Glutamine also reduced the production of tumour necrosis factor alpha, a factor found in infected blood.

I am currently a specialist registrar in paediatric surgery and was inspired to do this research while working at the Institute of Child Health, London, where I became interested in the problems of infection in surgical babies. There is now a multi-centre randomised controlled trial set up to look at the benefits of glutamine in surgical neonates.

"My proudest moment was winning the Peter Paul Rickham Prize for the best paper by a trainee at the 2002 British Association of Paediatric Surgeons Conference."

PUBLICATIONS

Irish Journal Medical Science. 2002 Jan-Mar; **171(1 Suppl 1):**9.

Wound Repair & Regeneration 2002; **10 (2):**A31.

PRESENTATIONS

Oral presentation at the Irish Society of Gastroenterology, Dublin, November 2001.

Oral presentation at the Sylvester O'Halloran Surgical Meeting, Limerick, March 2002.

Oral presentation at the joint meeting of the Wound Healing Society and the European Tissue Repair Society, Baltimore, May 2002.

NAME

Roger Lawther

TITLE OF STUDY

The role of matrix metalloproteinases (MMPs) in colonic anastomotic dehiscence

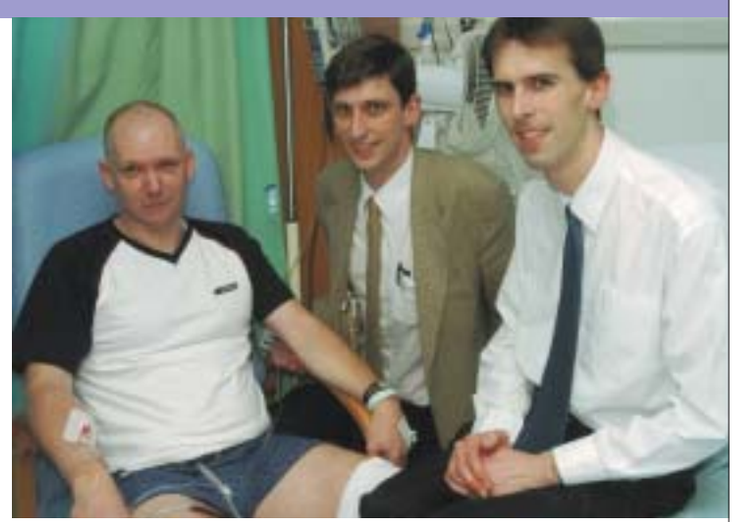
SITE OF WORK
Royal Victoria Hospital, Belfast

FELLOWSHIP/SPONSOR
The Frances and Augustus Newman Foundation

FURTHER FUNDING
Royal Victoria Hospital Research Fellowship

SUPERVISOR
Mr Keith Gardiner, consultant colorectal surgeon

Below: Roger Lawther (right) and his supervisor, Keith Gardiner (centre), with a patient who recently underwent a colonic anastomosis in the Royal Victoria Hospital, Belfast.



The joining of two segments of bowel together during an operation is known as an 'anastomosis'. This technique is used in the treatment of a wide variety of diseases. Satisfactory healing of an anastomosis is crucial to the success of these operations. Anastomotic leakage (also known as dehiscence) means patients usually need to return to the operating theatre for an emergency operation which involves the construction of a stoma. They have a significant increase in length of hospital stay and their risk of death is increased three-fold.

Collagen content within the bowel wall provides strength for an anastomosis. MMPs are a group of enzymes that degrade collagen. Their action is regulated by various agents especially tissue inhibitors of metalloproteinases (TIMPs). Our hypothesis was that in patients who are at high risk of anastomotic leakage, there is an imbalance between the expression of MMPs and TIMPs resulting in reduced collagen levels and weaker anastomoses. MMP inhibitors may then be used to correct this imbalance, maintain collagen levels, and prevent the complication of anastomotic leakage.

A laboratory model was successfully used to investigate the healing of small and large bowel anastomoses, with or without the presence of sepsis during the first three post-operative days. Our results were important in showing that excessive collagen degradation may not be responsible for dehiscence of septic large bowel anastomoses but that other factors such as impaired collagen synthesis may be more crucial. These findings will hopefully be useful in targeting new therapeutic strategies for improving outcomes in patients with septic large bowel anastomoses.

"The risk of death in patients who develop anastomotic leakage is increased three-fold."

PUBLICATIONS

The American Journal of Pathology 2003; **162:**1271–1282.
The American Journal of Physiology 2003; **284:**R1296–R1305.
Journal of Urology 2002, **168** 1615–1620

PRIZES

First Prize in Basic Science at the European Society of Paediatric Urology, 2002.
Urological Research Society Annual Prize, 2002.
Royal Society of Medicine Section of Urology Short Papers Prize, 2002.
First Prize in the Senior Catagory, Institute of Child Health Poster Competition, 2002.

PRESENTATIONS

BAUS Annual Meetings, 2001 and 2003.
Urological Research Society Annual Meetings, 2002 and 2003.
European Society of Paediatric Urology Annual Meetings, 2002 and 2003.
Renal Association Plenary Session, 2001

NAME
Nikesh Thiruchelvam

TITLE OF STUDY

The effects of urinary outflow obstruction on the developing fetal bladder

SITES OF WORK
Nephro-Urology Unit, ICH (primary site) and Division of Applied Physiology, Institute of Urology; University College London

FELLOWSHIP/SPONSOR
The Vandervell Foundation

FURTHER FUNDING
The Special Trustees of Great Ormond Street Hospital for Children NHS Trust.

Great Ormond Street Hospital for Children NHS Trust/Institute of Child Health Science Development Initiative Pump-priming Award

One of my supervisors, Peter Cuckow, received a Royal College of Surgeons of England Pump-priming Award to help in the purchase of radiotelemetry equipment used in this study

SUPERVISORS
Professor Adrian S Woolf, head of the nephro-urology unit, Institute of Child Health (ICH);

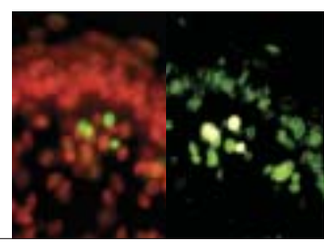
Mr Peter M Cuckow, consultant surgeon and honorary senior lecturer in paediatric urology, Great Ormond Street Hospital for Children and Institute of Urology

Professor CH Fry, professor of physiology, Institute of Urology

Posterior urethral valves affect approximately 1 in 5000 male births. They are the commonest known cause of end-stage renal failure in children. This study aimed to understand why the bladder develops abnormally with blockage of the urinary tract in infant boys with posterior urethral valves. Hopefully we can then develop better treatments for long-term problems caused by these urethral lesions (such as bladder maldevelopment and dysfunction) and renal failure.

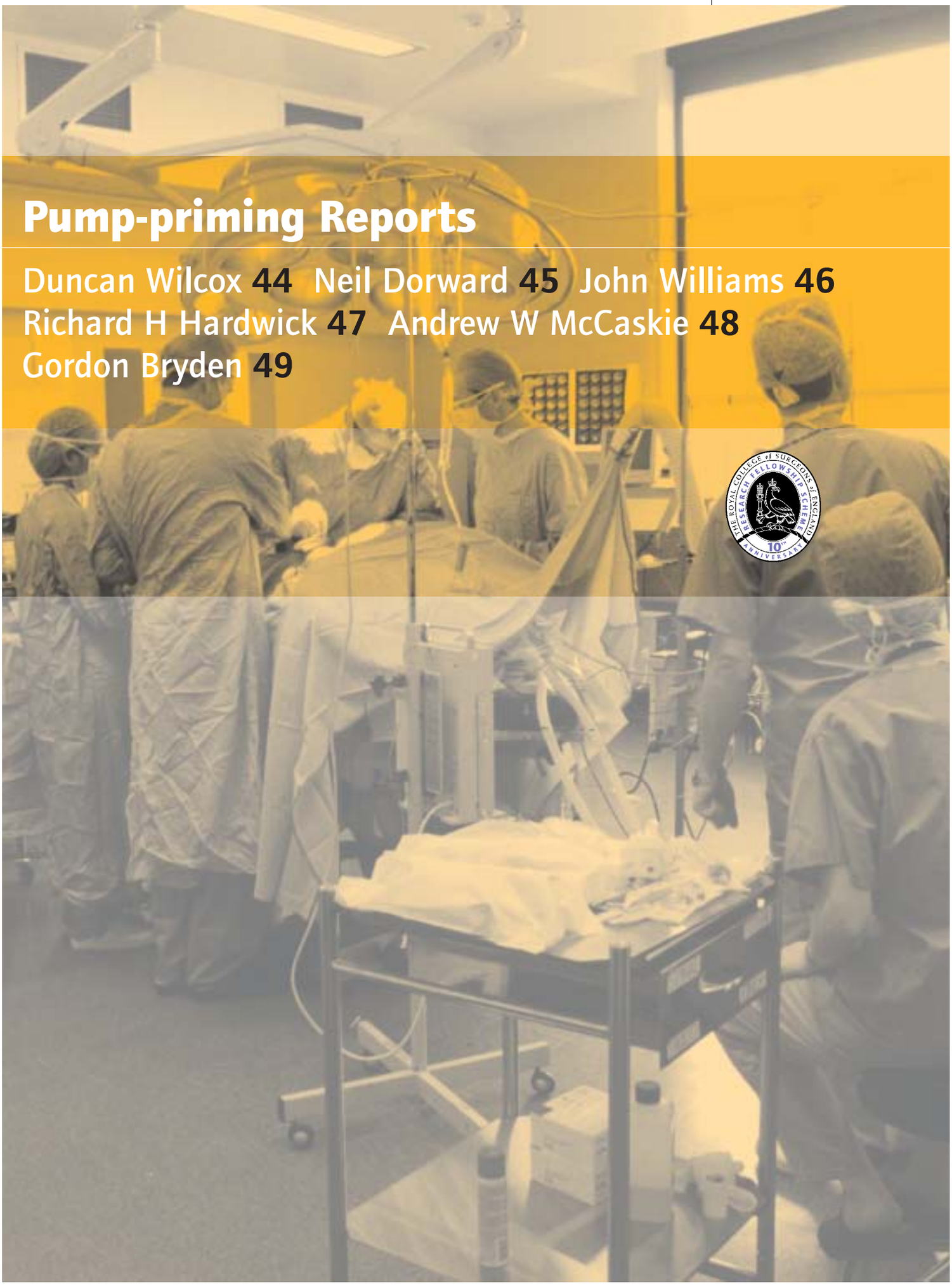
In an experimental model, I found that the developing fetal bladder became larger and heavier following urinary obstruction. This was because it had more multiplying, larger cells. Tests revealed that the obstructed bladder was able to produce much less force to contract and that neurotransmission was altered. I found that the obstructed fetal bladder produced less tone and was less elastic. I also observed an imbalance between multiplying cells (proliferation) and dying cells (apoptosis) and deregulation of the molecules involved in cell death.

Many boys suffer symptoms of bladder dysfunction, such as urinary incontinence, poor bladder emptying, urinary tract infections and bladder instability. In addition, many suffer from renal impairment requiring many hospital visits, repeated blood tests, medical therapy (with their subsequent side-effects), dependence on dialysis machines and some need to undergo major surgery (renal transplantation). Furthermore, in utero intervention, such as fetal cystoscopy and valve ablation, or simple bladder drainage by vesico-amniotic shunting, has done little to alter disease progression in these children. I hope, with further investigation, my research (which has led to the award of an MD) will ultimately lead to the development of novel strategies in the management of this condition.



Far left: Section of experimental fetal bladder shows apoptotic, dying cells (bright green) stained with propidium iodide and TUNEL-FITC and
Left: with TUNEL-FITC only.

"Posterior urethral valves are the commonest known cause of end-stage renal failure in children."



Pump-priming Reports

PUBLICATIONS

J Urol 2002; **167**:385–390.
J Paediatr Surg **38**(1):3–8.

PRIZES

British Association of Paediatric Surgeons Prize Essay 2002.
European Society for Paediatric Urology, Scientific Poster Prize 2001.

PRESENTATIONS

European Society for Paediatric Urology, 2001.
British Association of Paediatric Surgeons, 2002.

NAME

Duncan Wilcox

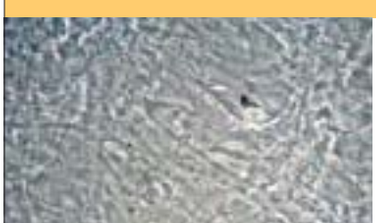
Consultant paediatric urologist, Guy's and Great Ormond Street Hospital

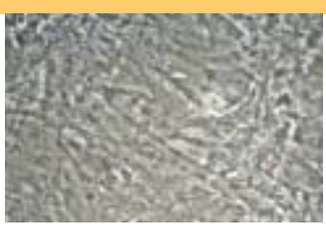
TITLE OF STUDY

Normal and abnormal bladder development

SITE OF WORK
Institute of Child Health, London

FURTHER FUNDING
Action Research





All images: Fetal detrusor smooth muscle cells grown in culture showing the typical 'hill and valley' appearance.

One in three boys born with bladder outlet obstruction will develop chronic renal failure before ending puberty. Bladder outlet obstruction is the commonest cause of chronic renal failure in children under five years. Fetal bladder outlet obstruction often also results in urinary incontinence.

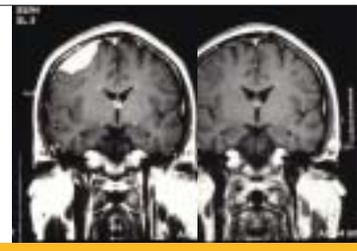
Abnormal bladder development, caused by the obstruction, is known to contribute to both these problems. The aim of this study is to understand normal and abnormal bladder development. It is hoped that manipulation of the abnormal development will allow normalisation of bladder function.

We investigated bladders at different points in normal development from early fetal to adult. Immunohistochemistry was performed on the bladders to identify the normal sequence of supporting cell structure formation. We also analysed the molecules that act as receptors and their quantity during development was studied. Subsequently, fetal bladders have been grown in culture dishes and using blocking molecules we attempted to asses the role of individual proteins in normal bladder development.

This is a long-term study, so far the department has had three research fellows who have worked in this field. We have started to identify the normal pattern of extracellular matrix development in the bladder and we are currently working on how manipulation of these molecules can alter bladder development. We hope to work on organ culture and isolated stretched and unstretched detrusor smooth muscle cells in the near future.

I am very pleased that the research project has been set up and now continues in an ongoing effort to reduce urinary problems in children. Research teaches us to ask questions about patient care in a scientific and critical way. This enables us to develop new management options but also to analyse other people's research so that we can use this information in the treatment of patients.

PUBLICATION
Journal of Neurosurgery 1998
88:656–662.



Left: Coronal scan images showing restoration of the normal cerebral architecture after removal of the tumour.

NAME
Neil Dorward

TITLE OF STUDY

Computer simulation of brain distortion by tumours

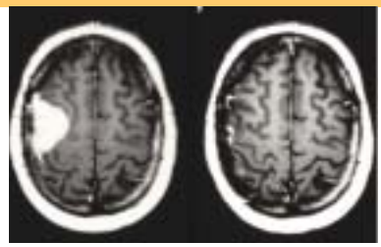
SITE OF WORK
Royal Free Hospital, London

Distortion of the brain leads to impaired function and thus paralysis of limbs, numbness or speech difficulties depending on the site of compression. This study aims to develop computerised simulations of brain distortion around tumours; investigate the resultant pressure effects and thereby predict these functional impairments in other clinical settings.

In this study I have used meningiomas as the model tumour to investigate. Meningiomas are progressive benign tumours that can cause epilepsy, limb weakness, numbness, speech difficulties and blindness depending on their location and the area of brain affected.

They occur on the lining of the brain and press in on the brain as they develop. Many can be removed surgically, restoring the normal architecture of the brain.

I selected a group of patients who had undergone surgery and who had normal post-operative scans. These scans can be used to define the mesh (computerised map of the brain scan) for both normal brain and the distorted brain with the tumour present. The relative movement of different regions of the brain can then be determined and the pressure effects simulated.



Left: The post-operative image was used to define the normal shape of the brain prior to tumour growth, which was then simulated by the computer programme.

A pilot study has been conducted that proves the feasibility of this method. In this study we were able to define a computer mesh for individual patient's scans and successfully simulate the distortion witnessed during the surgical removal of the tumour. The project continues with the mapping of tumours and measurement of the consequent brain shifts.

This study built upon my MS thesis, which included detailed measurement of brain distortions during surgery. The project is envisaged to continue with investigation of other tumour types and traumatic injuries.

"Meningiomas can cause epilepsy, limb weakness, numbness, speech difficulties and blindness."

PRIZES

Northern Region Registrars' Research Prize 2002.

PRESENTATIONS

European Orthopaedic Research Society meeting June 2003.

NAME

John Williams

Consultant and honorary clinical senior lecturer, orthopaedic surgery

TITLE OF STUDY

The role of vascular endothelial growth factor (VEGF) in bony metastases from breast cancer

SITE OF WORK

School of Surgical Sciences, Newcastle University

FURTHER FUNDING

The Wishbone Trust and Newcastle University Hospitals Special Trustees

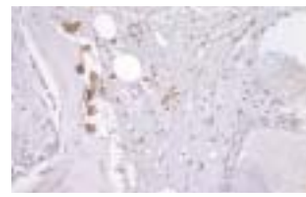
RESEARCHER

Stephen Aldridge clinical research associate
Freeman Hospital, Newcastle upon Tyne

When breast cancer spreads in the body, 50% of the new sites it moves to are in bone. Metastases are cancers that started in another area of the body but have spread. Once patients are diagnosed with bone metastases the disease is no longer curable. Skeletal metastases give rise to pain, hypercalcaemia, pathological fractures and can lead to spinal cord compression. Tissue staining techniques have shown that breast cancer cells that have metastasised into bone produce VEGF in large amounts.

This study aims to investigate VEGF expression by breast tumour cells in bone metastases and by osteoclasts (cells that surround bone metastases and are responsible for the breakdown of bone); the effects on osteoclasts in the laboratory; and the role of VEGF receptors on osteoclasts.

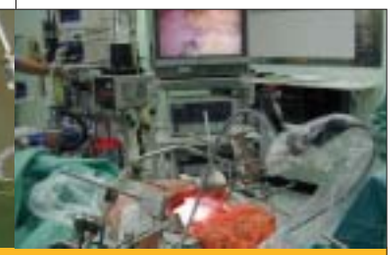
Preliminary findings in the laboratory indicate that osteoclasts can use VEGF in place of a growth factor normally involved in the differentiation of these cells. We have yet to investigate the effect of VEGF on the ability of osteoclasts to resorb bone.



Above: Stephen Aldridge (left) and John Williams
Above right and below: Serial sections of a specimen from a bone metastasis. A is stained for the osteoclast cell line marker CD68 and the corresponding serial section B is stained for Vascular Endothelial Growth Factor Receptor 1 (VEGFR1). It is possible to identify multinucleated cells staining for CD 68 in A and match them with the cells in B showing that osteoclasts express VEGFR1.

Our study may lead to the identification of a novel therapeutic approach to reduce the spread of breast cancer to bone and the complications associated with this.

Right: The LARTO T-bar in testing.
Far right: A LARTO in progress.



NAME

Richard H Hardwick

Consultant upper GI surgeon

TITLE OF STUDY

The development of laparoscopically assisted radical trans-hiatal oesophagectomy (LARTO)

SITES OF WORK

University Hospital of Wales, Cardiff

Addenbrookes NHS Trust, Cambridge

The aim of the study was to investigate the feasibility of using 'key-hole' cameras and instruments to assist in open operations to remove the oesophagus through the diaphragm without cutting open the patient's chest (thoracotomy).

Trans-hiatal oesophagectomy is one operation currently performed to remove oesophageal cancer. The oesophagus is dissected out of the chest from below through the diaphragm rather than through a cut in the chest. The advantage of this approach is that it reduces complications, however, access can be limited and vision poor. By using a 'key hole' camera (laparoscope) we hope to get better views of the surgical field and improve the safety and completeness of this operation. Special equipment was designed and made to help in this process.

A special T-bar was designed and made to act as a movable fulcrum for the laparoscope. It was apparent early on that this idea was of limited clinical value because the space available to position the T-bar was too small in most patients. Abandoning the device, we moved on to experiment with a single clamp for the laparoscope. This worked better but access was still difficult due to crowding of instruments. We next tried holding the laparoscope free without a clamp and this worked much better. To date, six patients have undergone a LARTO procedure and all have done very well. However, it is early days still and we continue to experiment with methods of improving access to and exposure of the oesophagus.

I was inspired to undertake this research due to a long-standing interest in the possibility of making trans-hiatal oesophagectomies easier, safer and more radical operations for oesophageal cancer. This is the beginning of a rolling programme to investigate potential improvements in operative technique for oesophago-gastric cancer. We will continue entering patients in the pilot phase of the study until we are happy with the tools and technique. Then we will perform a randomised prospective trial to test this approach.

Life for patients with oesophageal cancer is frightening and often short. Avoiding a thoracotomy is advantageous but doing this must not compromise the patients chance of a cure.

As a consultant upper GI surgeon I believe Pump-priming grants to be a good way for newly appointed consultants to get a research project started. I would highly recommend them to anyone.

NAME

Andrew W McCaskie

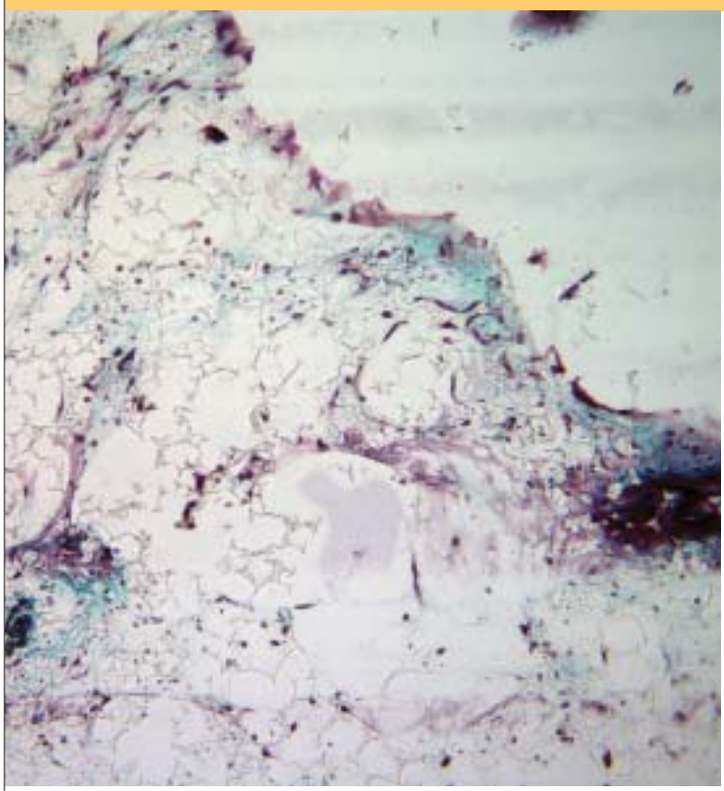
Professor of trauma and orthopaedic surgery

TITLE OF STUDY

The therapeutic application of stem cell technology in orthopaedic surgery: a biological repair system for bone and joints

SITE OF WORK

School of Surgical and Reproductive Science,
University of Newcastle



Left: Mesenchymal stem cells cultured in a porous biomaterial scaffold. Masson's trichrome and Von Kossa staining show numerous colonies of cells (purple) evidence of an extensive collagenous deposits (green) and production of a mineralized matrix (black), indicative of osteoblast function.

Stem cell research aims to produce a biological repair system for diseased or damaged tissues. This study aims to develop stem cell research in trauma and orthopaedic surgery by identifying adult (non-embryo) sources of these cells.

A system of informed consent was developed to enable adult patients undergoing total knee replacement to donate bone marrow released during surgery (this is normally discarded). Specific protocols were then developed to isolate and culture mesenchymal stem cells (MSCs) in the laboratory. MSCs have the ability to become bone forming cells, cartilage forming cells and fat cells. The ability to control this differentiation will allow future clinical applications to be developed. Further protocols were therefore used to drive MSCs into specific cell types.

We have successfully isolated and cultured mesenchymal stem cells and have been able to drive cell differentiation into the three cell lines: bone forming, cartilage forming and fat tissue. We intend to use these cells for laboratory cell biology experiments. Currently, we are focusing on tissue engineering applications that combine cell populations with scaffold structures as these have potential uses in correcting bone and cartilage defects.

NAME

Gordon Bryden (1965–2002)

TITLE OF STUDY

Development of novel model systems to study cellular interactions between prostate cancer and bone marrow stroma

SITE OF WORK

Royal Hallamshire Hospital

Alistair Gordon Bryden, a senior lecturer in urology at the Royal Hallamshire Hospital, Sheffield was awarded a College Pump-priming grant in 2001. Tragically, he died on 9 July 2002, aged 36, following a sports injury.

Gordon was born in Scotland in 1965. He gained a BSc in Medical Sciences at the University of St Andrews in 1987 and qualified in Manchester in 1990. He pursued his basic surgical training in London, Preston and Manchester, obtaining his fellowship from The Royal Colleges of Surgeons of England and Glasgow in 1994. He then entered higher surgical training in urology in Manchester in 1995, and became a clinical lecturer in 1997. Unlike most trainees, Gordon was able to undertake and complete an excellent research project on the biology prostate cancer without taking a period of full-time research. This culminated in the submission of a thesis to the University of Manchester, and the award of a doctorate's degree in May 2000. He obtained his CCST in 2001, before joining the Academic Urology Unit at the University of Sheffield as senior lecturer and honorary consultant urologist at the Royal Hallamshire Hospital. Gordon's ambition was to become a clinical academic.
He excelled in research, teaching and performed complex procedures, that few of us would tackle, with successful outcomes. His care and compassion with patients and their families were remarkable. He gave them the time they needed, rather than the time he had to spare. He took in charge organisation of the undergraduate teaching curriculum in urology and became involved in training of our junior doctors with considerable patience and dedication.

He was particularly interested in studying the mechanisms by which prostate cancer affects the skeleton and this work continues supported in part by the Gordon Bryden Charitable Memorial Fund which is open to donations largely through the generosity of individuals and industry, in his memory.

Freddie Hamdy Sheffield, *October 2003*

DONATIONS CAN BE MADE TO THE GORDON BRYDEN MEMORIAL FUND by sending cheques to: Mrs Carole Stenton, Academic Urology Unit, Royal Hallamshire Hospital K floor, Glossop Road, Sheffield S10 2JF, UK. Please make cheques payable to 'The University of Sheffield – Gordon Bryden Fund'.

In view of the tragic circumstances, the work undertaken by Gordon and Professor Hamdy has been continued by Josh Phillips, a research fellow in Sheffield in collaboration with Professor Kim Patterson's group at the University of Turku, Finland. The outcome of this work will feature in the next research report.

Preiskel Elective Prize

This prize is awarded to medical students wishing to pursue a career in surgery and who are planning to undertake their elective attachment in 'Surgery in the Developing World'.

James Goodman

St George's Hospital Medical School, London

LOCATION OF ELECTIVE

Tamale Regional Hospital, 'Binde' Rural Health Centre, Baptist Medical Centre and Saboba District Hospital, 'Northern Region', Ghana.

Ghanian children showing typical signs of Kwasmorkov and Umbillical hernia.

Shiva Dindyal

Imperial College, London

LOCATION OF ELECTIVE

Port-of Spain General Hospital, Trinidad.

Doctors with Shiva scrubbed up for a vascular surgery list.

Karen Woo

Royal Free and University College London

LOCATION OF ELECTIVE

Wewak General Hospital, Wewak, Papua New Guinea.

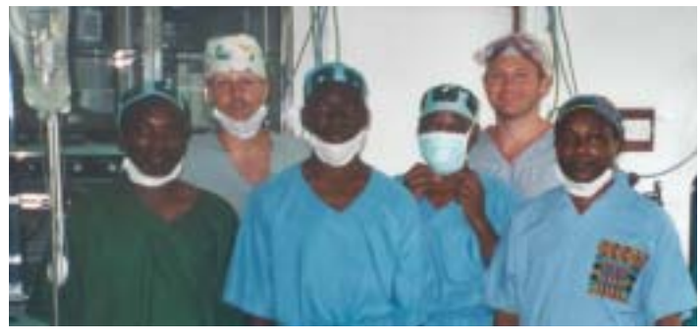
Karen with some local children in Wewak.

James Donaldson / James Baker

University College London

LOCATION OF ELECTIVE

Queen Elizabeth Central Hospital, Blantyre, Malawi



The orthopaedic team at Queen Elizabeth Central Hospital.

Matthew Gardiner

Oriel College, University of Oxford

LOCATION OF ELECTIVE

Nepal Medical College Teaching Hospital.

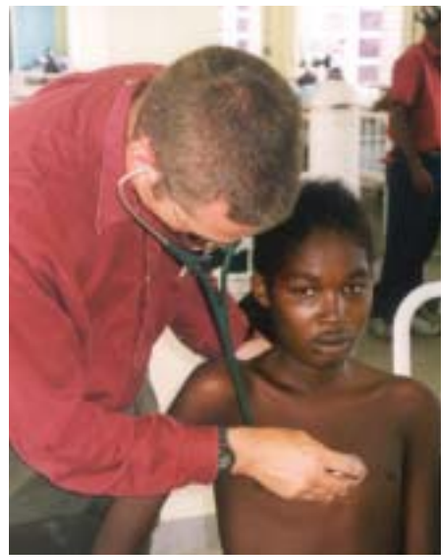
Matthew assisting with an open cholecystectomy.

James Hopkins

Guy's King's & St. Thomas' School of Medicine, London

LOCATION OF ELECTIVE

Georgetown Public Hospital and Remote Area Medical Volunteer Corps Local Health Post, Aishalton, Guyana.



James examining a patient at Georgetown Public Hospital

Clinical Effectiveness Unit (CEU)

The Clinical Effectiveness Unit (CEU) was established in 1998 as a collaboration of The Royal College of Surgeons of England and the Health Services Research Unit of the London School of Hygiene and Tropical Medicine.

The partnership between the College and the School was initiated on the basis of an external review of College's audit activities. The review recommended creating an academic partnership. The remit of this accademic collaboration was to carry out national clinical audits of surgical care, to produce evidence on clinical and cost-effectiveness and to develop and refine audit methodologies. Since April 2001, CEU staff have been involved in the development of clinical guidelines through input to the National Collaborative Centre for Acute Care, funded by the National Institute of Clinical Excellence, and hosted by the College.

During the first five years in its current form, the CEU has been very successful. Large-scale studies of the processes and outcomes of surgical care have been the core of the CEU's work programme. A number of these audit projects have been completed (**eg National Total Hip Replacement Outcomes Study, National Comparative Audit of Sino-Nasel Surgery**), whereas others have been initiated (**eg Subarachnoid Haemorrhage National Comparative Health Outcome Study, National Prospective Tonsillectomy Study**). *The staff capacity involved in national clinical audits has doubled in size.*

An important new initiative was the exploration of the usefulness of existing routine data bases for clinical audit, such as the **Hospital Episode Statistics system**, a data base that holds information about every admission in an NHS hospital in England. Another important step for the CEU and the College is the development of a central web-based system for data collection. Such a system allows local hospital units to enter their data directly into a central database located in the College. This development makes it possible for the CEU to respond quickly to requests from any party to initiate large-scale studies of the quality of surgical care.

The CEU has been able to expand its activities over the years, despite the loss of core funding from the Department of Health in 2001. At present, the *CEU receives about 20% of its annual income from the endowed research funds of the College, and all other income is derived from external sources*. As a direct consequence of these promising developments, the College has renewed the partnership agreement with the School, and agreed to support the CEU *for another 5 years until 2008*.

In the last year, CEU staff also obtained a number of personal grants. *Jan van der Meulen received a National Public Health Career Scientist Award from the NHS* to study the quality of surgical care. *Julia Langham was awarded an MRC Special Training Fellowship in Health Services Research. Christian Brown received a project grant from BUPA for his project on self-management for men with lower urinary tract symptoms, a project initiated through a RCS Research Fellowship. The North West*

Below: Saravana Ganesh, CEU research fellow, with cardiothoracic surgeons, Bob Bonser and Stephen Rooney at the Queen Elizabeth Hospital, Birmingham.

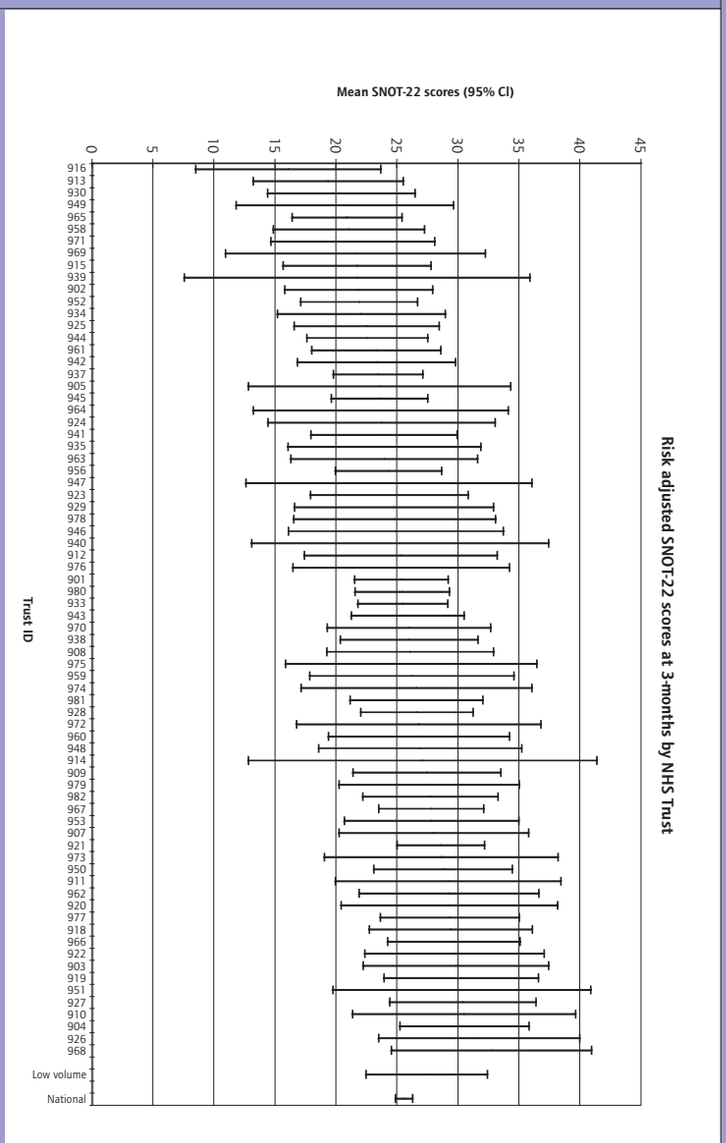
London Strategic Health Authority supported a project to evaluate priority scoring systems to manage waiting lists for elective surgery

Many projects of the CEU are co-ordinated by surgical research fellows who have a number of years of clinical experience. At present, the CEU has six fellows. Most of them will stay with the CEU for two years, during which they aim to complete a thesis for a higher degree. The fellows contribute to all aspects of the projects (project design and management, data collection, statistical analysis and reporting). They also receive intensive research training, very often based on the MSc teaching programme of the London School of Hygiene and Tropical Medicine.

As an example of the audit work that the CEU carries out, a few key features are described of the National Comparative Audit of Sino-Nasel Surgery that produced its final report in the Summer of 2003. This audit was initiated in 1999 in close collaboration with the British Association of Otorhinolaryngologists – Head and Neck Surgeons. Sinonasal surgery is carried out for chronic sinusitis and nasal polyps. Both conditions can be very unpleasant and reduce the patient's quality of life. Surgical treatment is often the last resort for these patients. There are currently many different operations being used for the treatment of sinonasal disease, and it remains unclear if some achieve better long-term outcomes.

All hospitals in England and Wales undertaking sinonasal surgery were asked to participate. **The willingness of surgeons and patients to participate was high: 92% of the ENT surgeons and 99% of the patients agreed to take part**. The audit was funded through contributions of participating trusts (**£600 from smaller and £1200 from larger trusts**).

As a consequence of these funding arrangements, only **57%** of the invited trusts accepted the invitation to participate. In other words, a funding arrangement for audit projects based on contributions from the participating hospital seem to have a detrimental effect on their willingness to participate, which is, in addition to the considerable administrative burden, an essential argument against it.



Left: Dr John Browne, lecturer in outcome assessment, CEU, teaching on the research methods course in Hong Kong.

Clinical data were collected over a period of six-month period in 2000 on 3,128 patients undergoing sinonasal operations in 80 participating NHS Trusts. All patients were followed up for 12 months to monitor their symptoms after surgery. Surgeons completed a questionnaire at the time of operation and patients completed questionnaires before surgery, and at 3 months and 12 months after surgery. The main outcome in the study was the patient's symptom status as measured with the Sinonasal Outcome Test, a questionnaire with 22 questions (SNOT22).

The key issue in the analysis of the results of any audit is that of trying to explain variability among the hospitals. Three sources of variability can be distinguished: 'case mix', random variation, and differences in the way that the surgical procedure is performed. The figure shows the mean SNOT22 scores at three months after surgery for all participating trusts.
The results are adjusted for 'case mix', a term that is used to indicate differences in the characteristics of the patients that are known to modify the risk of surgery. This implies that we have eliminated as much as possible the effect of case mix as an explanation for the variation in outcome. The vertical bars for each observation represent the '95% confidence interval'. The confidence intervals represent the uncertainty in the mean SNOT value due to random variation, and these depend largely on the number of patients treated in each trust. The graphical representation of the results with the confidence intervals is often called a 'caterpillar plot' for obvious reasons. The figure illustrates that the interpretation of the results of an audit is often difficult and that it is not easy to identify 'outliers'. To think about the magnitude of this problem, it is important to think about the chance that a unit with divergent results is indeed an outlier. In many cases, its extreme position will be due to random variation. **The only constructive way forward is to see audit results, such as those presented here, only as an invitation to review performance, and not as a way of identifying directly trusts in which surgical care is poorer than can be expected.**

The National Collaborating Centre for Acute Care: The Good

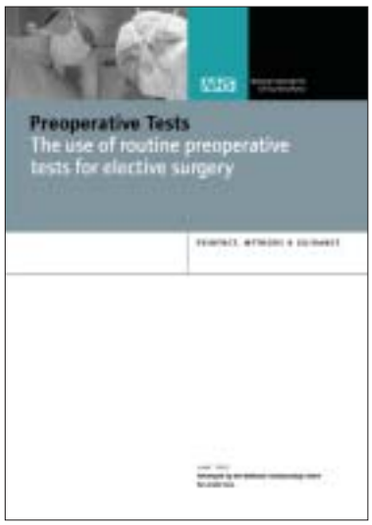
The Bad

and the (not so) Ugly

The National Collaborating Centre for Acute Care (NCC-AC), based at the Royal College of Surgeons, is a virtual centre that is home to a multi-disciplinary health services research team. The Centre was established by the National Institute for Clinical Excellence (NICE) on 1 April 2001 to develop clinical guidelines on its behalf. The Centre comprises a partnership between a variety of academic, professional and patient-based organisations.

What we have accomplished?

The NCC-AC has completed two guidelines, those for routine pre-operative testing and those for the early management of head injury. The entire process has been one of close collaboration with a wide range of individuals and groups, including representatives of key stakeholder groups who gave their time to sit on the respective **Guideline Development Groups, and staff at NICE and the Modernisation Agency**.



Above: Guidelines produced by the NCC–AC

Additionally, we are working with the **Scottish Intercollegiate Guideline Network** on guidelines for the diagnosis and treatment of lung cancer. Although SIGN and the NCC-AC are sharing the work of completing a rigorous systematic review, each organisation has their own Guideline Development Group that works autonomously in designing the clinical questions to guide each study and the subsequent recommendations arising from a review of the evidence.

Further collaboration is occurring with regard to our work on the guidelines for dental recall. In this instance we are working with the **Cochrane Oral Health Group** in order to complete a systematic review on the clinical and cost-effectiveness of dental recall intervals.

We have recently commenced on a guideline for nutritional support.

What we have learnt?

During the past two years we have learnt that systematic reviewing can be a long and tedious process, and that we need to ensure ample time and resources are available to do a thorough review of the evidence. We have found that sometimes, decisions have to be made in the absence of published evidence. *This emphasises the importance of the knowledge and experience of patients and clinicians in developing recommendations.*

Our experience has shown us that participation of stakeholders is vital from the beginning stages of guideline development and that keeping the process of guideline development transparent contributes to the understanding and acceptance of guidelines. It is obvious that NICE

and the Department of Health recognise this as well. That is, NICE has recently adopted the practice of hosting stakeholder meetings during the scope consultation period in order to explain the process of guideline development. Furthermore, the Department of Health has recently piloted a web-based form so that individuals can more easily submit topics for guideline development.

The Good

We have a great team of staff in place who are well-trained in conducting systematic reviews. We have ensured that a team-working ethos is in place given that systematic reviewing can be a long and tedious job. It is important to share the work and ensure individuals are supported accordingly and not working in isolation. **A strong team ethos has also been developed when working with all individuals and organisations, including other Collaborating Centres, NICE, Guideline Development Groups and stakeholders.**

Above: Staff of the NCC–AC.

We have had positive experiences of recruiting representatives from professional and patient organisations to sit on the Guideline Development Groups and the input from both has been instrumental in ensuring sound guideline development.

Technical support from NICE has been extremely helpful. They have aided our staff in training for systematic reviews, with a writing course being developed for 2003. Co-operation with writers and editors at NICE have ensured the production of readable and coherent guideline documents.

The Bad (but improving)

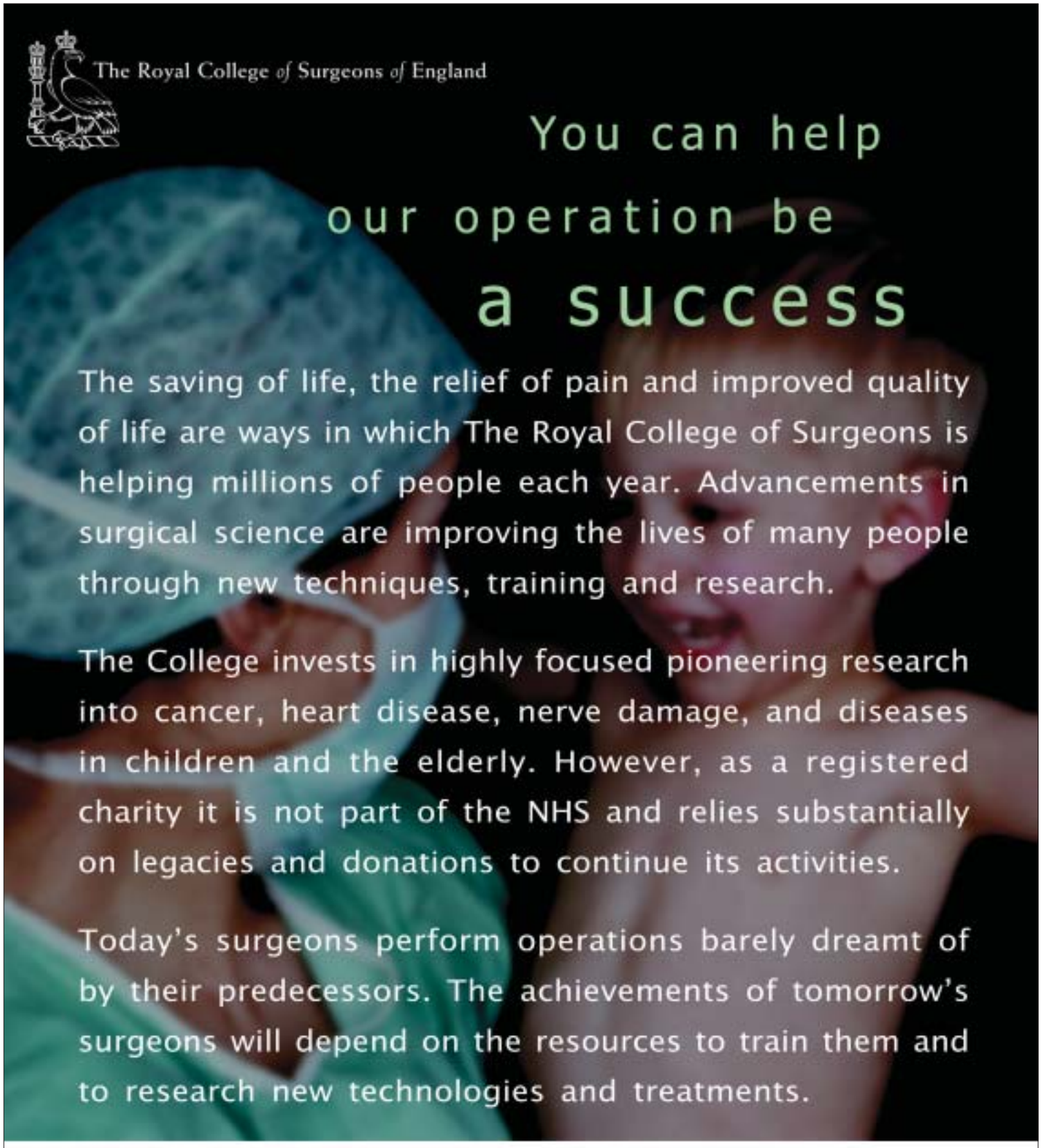
We still struggle with how to pick the most important issues on a topic and thus keep the scope of a project manageable. It is important to produce a high-quality guideline within a reasonable time frame, which must mean focusing on a key set of questions and not straying beyond a workable scope.

The Ugly (but getting prettier)

We have often found that deadlines are too tight and sometimes inflexible when it comes to delivering the goods on time. For instance, a body of literature can turn out to be much larger than originally anticipated. We are learning how to focus the clinical questions we want answered as much as possible. However, it has also become apparent that at times flexibility with timelines is required in order to allow sufficient time to complete the necessary work to a high standard.

Conclusions

We are learning what lends itself to a smooth guideline development process, and what does not. At the end of the day, we all have the same goals in mind – improved patient outcomes and quality of care. One of the main lessons from the past two years is that early communication between *all* stakeholders that continues throughout the entire process of guideline development and implementation is the key to achieving these goals.



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