The Bulletin

of the Royal College of Pathologists

Number 200 October 2022

In this issue: Celebrating the people and specialties of pathology

Also in this issue:

The Royal College of Pathologists
Pathology: the science behind the cure

Pathology: at the heart of your health
Celebrating our Diamond Jubilee

The Royal College of Pathologists
6 Alie Street, London E1 8QT

T: 020 7451 6700
E: info@rcpath.org
www.rcpath.org

The Royal College of Pathologists
Pathology: the science behind the cure

CONTENTS

OCTOBER 2022 NUMBER 200

On the cover:

The Diamond Jubilee *Bulletin* issues have focused on the diversity of the pathology specialties. The cover image represents some of these specialties.

EDITORIALS

From the Editor

Dr Shubha Allard

Welcome to the October *Bulletin*, which is our 200th issue and also the last of the four issues during the College's Diamond Jubilee year. This has been a memorable year for so many reasons but in particular for the death of Her Majesty Queen Elizabeth II, who was also our College patron. The national outpouring of grief reflected her exemplar life as our monarch and her extraordinary contributions to the country and the wider world.

The College held its first Open Day in September 2022, marking an important landmark for our relatively new home in Alie Street. Dr Suzy Lishman's enthralling 'Living Autopsy' was followed by interactive displays by consultants and trainees, both medics and scientists who captivated several young minds from school years 10–12. Many pathology subjects were covered in an engaging manner, with a rhinoceros' skull being part of a memorable veterinary pathology display. The College's 2021–2022 *Annual Report*, which will be published in November, will provide a summary of the many other lively events held during the Diamond Jubilee year.

This *Bulletin* issue culminates the Jubilee year with the important theme of 'Celebrating the people and specialties of pathology', adding further profiles and overviews showcasing our specialties. There are notable individuals and articles within the relatively wide fields of virology (p 706), haematology (p 697) and transfusion (p 703), but there is also recognition of less well-known fields such as forensic veterinary pathology (p 693).

We certainly need to look after and nurture our trainees with an inclusive teaching environment, tackling as many barriers to learning as possible. You will no doubt find the article on neurodiversity and specific learning difficulties highly informative, highlighting the need to recognise these conditions in training and the workplace (p 712).

We also need to support our educators. A timely meeting of Training Programme Directors in the East of England shared best practice and explored further training opportunities across pathology specialties (p 738).

It is gratifying to see initiatives aimed at engaging medical undergraduates in pathology research (p 715). There are tips and advice for others interested in creating a supportive research environment for students and helping them to develop technical skills, critical thinking and problem-solving, together with communication skills and team working.

We have many interesting articles in our Working Smarter section. Drs Taze and Griffin led a College survey that demonstrated variation in histopathological reporting of temporal artery biopsies for giant cell arteritis with potential for a standardised reporting protocol (p 719). Claire Verrill and colleagues demonstrate the benefits of using digital pathology to enhance histopathology–surgery–radiology case-based reviews following radical prostatectomy with many shared learning opportunities (p 722).

Digital morphology further offers an opportunity to harness artificial intelligence (AI)-based recognition. Marlene Correia and co-authors discuss the potential for application in feto-maternal haemorrhage estimation to support the prevention of RhD haemolytic disease in fetus and newborns (p 728).

As the use of digital pathology and AI become more embedded within the infrastructure across services, members of the College's Lay Advisory Group provide a timely reminder of ethical implications and the need to ensure meaningful engagement of patients and the public (p 718).

A new national programme for genetic testing and cardiological screening after sudden death highlights a key step forward towards prevention of further fatalities among families (p 724). Emma McCargow describes an innovative programme by Genomics England towards personalised healthcare utilising multimodal data in cancer diagnosis and research (p 727).

Returning to the theme of people, we describe initiatives linked to eminent pathologists including Dr Elizabeth Stokes' legacy and donations in microbiology (p 734), the William Tong prize in virology (p 732) and the Dacie–Wilkinson lecture as a collaboration between the College and the British Society for Haematology (p 739).

During the College's Diamond Jubilee we have tried to stay true to our pledge, through the *Bulletin* and other activities, to celebrate the pathology specialties and the people who represent the breadth of our remarkable workforce. We have certainly showcased the collective efforts needed for the delivery of pathology services to support patient care, with due attention given to research and innovation together with education and training, helping ensure the legacy for future generations.

Dr Shubha Allard
***Bulletin* Editor**

RETURN TO CONTENTS

From the President

Professor Mike Osborn

I am sure, like me, you were saddened by the death of Her Royal Highness Queen Elizabeth II on 8 September. The death of Her Majesty was particularly poignant for us as a royal college because the Queen was our patron – a role she took up in 1970 when the College received its Royal Charter.

Her Majesty visited the College three times during her reign, each time in her role as our patron, and each time at our previous building in Carlton House Terrace. The first of these visits was on 10 December 1970 when Her Majesty came to formally open the building.

The Queen, together with His Royal Highness Prince Philip, Duke of Edinburgh, visited the College for a second time on 19 February 1987 as part of the College's Silver Jubilee celebrations. Her Majesty and His Royal Highness again visited on 16 February 1994 to mark the re-opening of the College's premises at 2 Carlton House Terrace following major renovation. On their second and third visits, The Queen and Prince Phillip signed our visitor's book.

Having sadly lost Her Majesty as our patron, we will in time be granted a new royal patron. The exact process by which this will happen is as yet unclear at this early stage and it seems likely all Her Majesty's 600 or so patronages will pass to King Charles III who will then likely distribute them among other members of the Royal Family. We shall wait and see who will be our new patron. But, whoever it is, the College will work closely with them to champion pathology and the needs of our members to ensure we can provide the best care possible to our patients.

Our Open Day

Since my last article the College has been extremely busy. Our Open Day, a flagship event in our Diamond Jubilee celebrations, was moved to September when our previous plans for June were postponed because of rail and tube strikes. At the Open Day, as part of our work to further public education in the field of pathology (a core objective stated in our Royal Charter), we were delighted to be joined by 65 14–18-year olds from local schools. Our aim was to interest them in science and medicine as possible careers. The pupils came from Leytonstone School, Central Foundation Girls' School and Eastbury School.

We were also joined by Her Royal Highness, Birgitte Eva van Deurs Henriksen, Duchess of Gloucester, and Mr Leslie Morgan OBE, Deputy Lord Lieutenant for Tower Hamlets (the borough in which the College building is located).

Professor Sarah Coupland, Vice President for Communications, and I introduced the Duchess and Deputy Lord Lieutenant to members, honorary officers and members of the Trustee Board in the members' area. The Duchess of Gloucester unveiled a plaque to mark the 60th anniversary of the College (which is available to view in the members area) and signed the College's visitors' book. The Duchess of Gloucester, along with the Deputy Lord Lieutenant, the school students and their teachers, attended a fascinating 'Living Autopsy' session brilliantly given by Dr Suzy Lishman CBE, past President of the College (2014–2017).

In the afternoon, following lunch kindly sponsored by the Pathological Society, the students took part in nine interactive pathology-related activities. These were delivered by members from different pathology specialties and there was a range of activities offered. With quizzes from chemical pathologists, interactive sessions based on blood transfusion and video demonstrations around post mortems in rhinos and atherosclerosis in meerkats (who knew they can have hypercholesterolaemia?), not to mention the origami and 3D organ printing sessions, a great time was had by all who attended and we had fantastic feedback. A huge thank you to everyone involved.

In the evening of the Open Day, sponsors and key partners showcased their work to guests at our annual dinner. A big thank you must go to our sponsors Sonic Healthcare UK, Aiforia, Sectra, Smart in Media, Agilent and the Pathological Society, and to our partners 3D LifePrints and LabTests Online, without whom we could not have hosted this fantastic Jubilee Open Day event.

The annual dinner was our first since 2019. Guests included policymakers, stakeholders and College members who have worked with and for the College over the last three years. During the dinner, we announced the winners of the 2022 RCPath Achievement Awards, which celebrate excellence in pathology practice, education and training. I was delighted to present awards to four deserving teams from the Centre for Diagnosis and Research in Cancer, University of Colombo, Derbyshire Shared Care Pathology, iHistopathology and the UK Expert Haematology Panel on VITT (vaccine-induced immune thrombocytopenia and thrombosis). You can read more about these fantastic teams and their great work on our website.

Our Diamond Jubilee

Other events to celebrate our Diamond Jubilee this year are ongoing with a variety of activities all around the country. In late September, pathologists from a variety of specialties, together with other enthusiasts, cycled from Lands End to John O'Groats over a period of 12 days. The event was a combined venture between Cancer Research UK (CRUK) and the Royal College of Pathologists, sponsored by Sonic Healthcare UK and organised by Cycle Retreats. Facing terrible weather, wind, rain and climbs cumulatively greater than the height

RETURN TO CONTENTS

Professor Mike Osborn joined cyclists Professor Sarah Coupland, Rachel Brown, Aditya Shivane and Marin Gill at the start of their Land's End to John O'Groats bike ride.

of Mount Everest, the 21 participants and the team raised over £37,000 for CRUK, a hugely worthwhile charity with whom we work extremely closely to highlight workforce issues in pathology.

Together with Lance Sandle, our Registrar, I was lucky enough to meet the team at one of their stop overs in Warrington. Peter Johnston, Vice President for Professionalism, and Dr Rachael Liebmann OBE from Sonic Healthcare met the team when they finished in John O'Groats. This was a fantastic achievement, a great advert for the College and a superb addition to our Jubilee celebrations. Congratulations and thank you to all involved but particularly to our sponsors and to Professor Sarah Coupland, Vice President for Communications, who not only organised this event (as well as many other elements of the Diamond Jubilee celebrations), but also took part. Well done Sarah. You can find out more about the ride and see pictures on our website and donate here.

Pathology Summer School

In August, the 2022 Pathology Summer School took place and was sponsored by the College and our partners, including the British Division of the International Academy of Pathology, the Pathological Society, British Society for Haematology, Association of Clinical Pathologists, the British Infection Association and the British Neuropathological Society. This was the first in-person event for three years and it was a huge success, with around 70 medical students from across the UK joining us for the event. The Summer School offers UK medical students the chance to discover more about pathology and its role in healthcare with the aim of tempting them into pathology careers.

I was delighted to welcome students and introduce them to the different pathology specialties. There were also lectures from our Vice President for Professionalism, Professor Peter Johnston, as well as other colleagues on a wide range of topics, including pathology training and the day-to-day activities of a pathologist. Interactive breakout sessions gave students the chance to discover more about our various pathology specialties while working in small groups with fellow students. Planning has already started for next year's Summer School, which promises to be extremely popular.

The Pathology Portal

The College, in collaboration with Health Education England (HEE) and other professional bodies, proudly launched the Pathology Portal in August. Professor Jo Martin, past President of the College (2017–2020), together with a group of specialty editors and many trainees, have worked, and continue to work, tirelessly on this important project.

The Pathology Portal is a new and free-to-use educational resource for trainees, practising pathologists, scientists and those in pathology-linked roles, and open to all College members. The Portal includes over 2,000 online interactive resources developed to deliver high-quality and intriguing training materials. They can be customised to individual needs, used to support flexible and return-to-work training, and test learning. There is a wide mix of pathology staff accessing the Portal, covering a variety of subspecialties.

The Portal is continuously growing – the uptake so far has largely been within histopathology, neuropathology, cytology and autopsy, but other disciplines are being prepared for live release, including haematology, and we are very keen for the Portal to house material from all our specialties.

In addition to pathologists and allied professionals other potential users can also ask for access to the resource, for example an ophthalmologist who is looking to learn about adnexal tumours around the eye, as well as endoscopy nurses who are exploring content around biopsies. You may find some of the content helpful in supporting the training of clinicians you work with. The number of users is increasing daily and we have had superb feedback. One trainee said, "The Pathology Portal has been helpful in making ST1 less stressful!" We hope to make learning or filling knowledge gaps less stressful for everyone. Please see our website for information about the Portal and how to access it.

Representing our members

Over the last few month the College has been lobbying for the needs of pathology and for resources to support you to provide the highest level of care possible for patients. We live in turbulent times, with repeated and rapid changes in government having taken place over the last few years and indeed months. However, our message has remained the same – pathology underpins all healthcare and pathologists, laboratories and departments need adequate resources and workforce to provide the pathology services required. Without these we cannot deliver what is asked of us.

We attended both the Labour and Tory Party conferences in Liverpool and Birmingham.

RETURN TO CONTENTS

With other royal colleges we attended the Academy of Medical Royal Colleges' Fixing the NHS events and discussed the importance and needs of pathology and pathologists with parliamentarians, policymakers and other stakeholders. These events were well attended and well received. They helped elevate our profile as a royal college and professional body and are another step in getting our message across and our voice heard.

Professor Sarah Coupland, Vice President for Communications, attended the event at the Labour conference where she was joined by Feryal Clark MP and the Special Adviser to Wes Streeting MP, Shadow Health Secretary. Feryal Clark MP delivered the closing remarks on the pressures facing the NHS and Social Care and the short and long-term solutions that can make a difference for patients.

I attended the roundtable events at the Conservative party conference to advocate for pathology services and raise pressing workforce issues. Lord Bethell, Former Parliamentary Secretary of State for Health and Social Care, delivered the opening remarks to stimulate discussion and there were some useful insights spanning workforce, integration, tech and patient access and experience. I also met Matt Warman MP who has a particular interest in innovation and technology. We will continue to work with these politicians to highlight the importance of diagnostics in healthcare.

In addition to the party conferences, the College represented you at numerous meetings with senior NHS staff including Amanda Pritchard, Chief Executive of NHS England, and Steve Powis, National Medical Director for England. Other honorary officers, including the chairs of the devolved nations, are in regular contact with NHS leaders and policymakers in all areas of the UK. I will be visiting Northern Ireland, Scotland and Wales in the near future to again raise the issues important to members, particularly around resourcing pathology.

In November I will be speaking in Westminster about resourcing cancer diagnosis and treatment. I will use that opportunity to stress once again the importance of an adequately funded and properly staffed pathology service. Because of our lobbying work, which involves both members and staff across the College, the groups and individuals who lead on healthcare policy and resourcing are gradually coming to better understand the needs of pathology. I truly believe our message is getting through, however we live in hard times and we must continue to highlight the issues important to us.

Your College, Your Profession tour

At the end of September we held the first of our Your College, Your Profession national engagement tour events in Plymouth. This was well attended by a range of members and trainees, from different specialties and stages in their careers. The group first discussed issues around workforce and resourcing. They provided helpful examples of not only problems faced by members, but also of solutions that have worked for them and suggestions of other possible solutions either for the College to implement or raise with policymakers. This was particularly useful since the NHS England Regional Lead for Pathology Services attended the first part of the event. While we were unaware he was planning to come, he made very useful contributions and was a great addition to the event and discussion.

The second half of the event focused more on what the College does well, what it could do better and how it could provide services more tailored to the needs of our members. Again, there was a useful, frank and helpful discussion and we have certainly learned a great deal from just this first engagement event.

We have more engagement events booked around the whole country, with meetings in Glasgow, Aberdeen, Belfast, Bodelwyddan, Newcastle, Norwich and London – and that's just the ones before Christmas. In the New Year we will host more in-person events and these will be supported by online meetings, to ensure everyone has the opportunity to be involved in the discussion. I would urge everyone to try and attend one of the in-person events or, failing that, an online forum. Details are on the website. We also have a dedicated email address for your suggestions on how the College could better engage with members and provide the services and support you need. Please do email your comments, suggestions and ideas to mycollege@rcpath.org

Haematological malignancy diagnostic classifications

Finally, for those of you whose work includes haematological malignancies, you will be aware that there have been some recent issues regarding updated diagnostic classifications in haematological oncology. The publication of two new haematological malignancy diagnostic classifications – the World Health Organisation (WHO) 5th edition and the International Consensus Classification (ICC) – is expected soon. The outlines have recently been published in *Leukemia* and *Blood*, respectively. While for the most part they agree and overlap with each other, the two classifications do differ in some areas.

The British Society for Haematology (BSH) and British Lymphoma Pathology Group (BLPG) have been asked to help with this issue and want to provide some interim guidance for members, while planning formal definitive guidance. Please see here for further the guidance.

To finish, I would like to thank you all for your ongoing hard work, often in difficult circumstances, and to wish you all a great autumn, and a happy festive season.

Professor Mike Osborn
President

RETURN TO CONTENTS

CELEBRATING THE PEOPLE AND SPECIALTIES OF PATHOLOGY

Shubha Allard

In our last Diamond Jubilee *Bulletin* issue, we continue to have excellent engagement from colleagues in response to our call to celebrate our pathology specialties and the people who work so tirelessly across the board.

So far, the January 2022 issue included profiles of some notable pathologists and their achievements, such as past Presidents Professor Jo Martin and Dr Suzy Lishman CBE. The April and July issues featured highly informative articles on the history, achievements and current work of many of our specialties. We further profiled consultants and trainees across many disciplines, celebrating medical and scientific achievements in the UK and abroad.

The October 2022 issue – as the final edition during the College's Diamond Jubilee year – now helps complete this theme. We start with a profile of Professor Sir Jonathan Van-Tam who became a very familiar face during the COVID-19 pandemic as England's Deputy Chief Medical Officer (CMO).

As the mark of a great man, he rather humbly describes his career starting out as having "scraped into medical school at the University of Nottingham in 1982". After being appointed as a clinical senior lecturer in public health and a consultant epidemiologist in 2002, his journey has involved wide and varied roles in the private and public sector, culminating in his high-profile post as Deputy CMO advising the government with some rather engaging media appearances.

> Pulling together the various contributions towards these celebratory articles has been an uplifting and humbling experience.

While he notes his military MBE in 1998 and being awarded a Knighthood in 2022 as particular career highlights, there are clearly so many other notable achievements. It is, however, good to hear him state that "helping younger doctors and scientists with their leadership development and career progression is what really gives me a buzz, more than all the glitz".

We are also very pleased to profile Dr Noha El Sakka OBE, who started her career in clinical pathology in Egypt and then moved to the UK where she completed her postgraduate training in medical microbiology and a PhD at the University of Aberdeen. She was appointed Director of Microbiology and Virology service soon after her challenging first consultant post and then in 2018 as Specialist Advisor to the Scottish government. She played notable national and regional roles in Scotland during the COVID-19 pandemic. Her efforts in the face of adversity are clearly remarkable and she has recently been awarded with an OBE for her services to the NHS and the COVID-19 response.

Noha is also the current chair of the Scottish Diagnostic Virology Group, which has been active for more than 60 years. It is appropriate during the College's Diamond Jubilee year to have a valuable reflection on the history of this group showcasing how scientific virology has risen to the many emerging challenges and has truly evolved with many successes.

I greatly enjoyed reading the article on veterinary forensic pathology by Professor John Cooper who works closely with his wife and colleague, animal law specialist Margaret Cooper. The article explores six decades of advancement with the subject now being a notable inclusion in training and the practice of pathology. The authors also highlight that the College has been true to its aims when founded 60 years ago in supporting the evolving specialties of pathology and welcoming members of the veterinary profession into its ranks.

Professor Jane Apperley, together with Harry Robinson, in their highly informative review on chronic myeloid leukaemia summarise discoveries from the 1960s to the modern day, including targeted therapies that have remarkably 'restored the life expectancy of most patients to that of the normal population'.

They rightly acknowledge many of the giants in the field but also highlight the great achievements that are feasible with close collaboration between pathologists, clinicians and the pharmaceutical industry striving together towards patient benefit.

We then move on to the article by Professor Marie Scully and Dr John-Paul Westwood entitled 'Thrombotic thrombocytopenic purpura: past, present and future'. This is a rare disorder but well recognised in its remarkable pathophysiology with microvascular thrombi associated with thrombocytopenia and haemolytic anaemia with fragmented red cells on blood film examination.

The authors indicate how far we have come since the description of the first fatal case in 1924 by Moschcowitz to now understanding the role of ultra large von Willebrand Factor (VWF) multimers and the VWF-cleaving metalloprotease in classification of the subtypes of thrombotic thrombocytopenic purpura. They review the

RETURN TO CONTENTS

evolution of therapies from steroids to plasma infusion and exchange, to more aggressive immunosuppression with rituximab (an anti-CD20 monoclonal antibody), to the use of the anti-VWF nanobody caplacizumab. Caplacizumab is the current standard of care in the acute thrombotic thrombocytopenic purpura pathway in the UK.

> We can take great pride in the collective contribution of so many individuals making a real difference to patients.

Finally, the current year also marks the 20th anniversary of the Systematic Review Initiative (SRI) and here we celebrate its exceptional contribution to developing the evidence base in the field of transfusion medicine. Susan Brunskill and Lise Estcourt highlight the SRI's critical role in driving forward scientific research that supports clinical practice, including appropriate use of blood towards patient safety and donor care.

The authors are rightly proud of the collective achievements of this programme. It has addressed more than 70 systematic review questions, often using complex statistical methodology and network meta-analysis, with publication of over 240 articles in peer-reviewed scientific journals. They have included helpful examples where the SRI initiatives have made a difference within transfusion medicine, emphasising the collaborative approach needed to identify the key topics subjected to critical scrutiny.

Pulling together the various contributions towards these celebratory articles has been an uplifting and humbling experience. We can take great pride in the collective contribution of so many individuals making a real difference to patients.

However, as we look ahead to yet more challenging times, we all need to strive to maintain a work–life balance and I would like to end by pulling out a quote from Professor Sir Jonathan Van-Tam's profile. His concluding sentiment is valuable advice for us all: "... remember your roots, who ultimately you are here to serve, and stay grounded".

Dr Shubha Allard
***Bulletin* Editor**

RETURN TO CONTENTS

PROFILE: PROFESSOR SIR JONATHAN VAN-TAM

Professor Sir Jonathan Van-Tam earned nationwide fame for his work during the COVID-19 pandemic as England's Deputy Chief Medical Officer and his media appearances during the Government's public health briefings. Prior to this, Sir Jonathan held numerous positions in the private and public sectors, focusing on the study of vaccines and the epidemiology of respiratory viruses. In this profile, we hear about his many career highlights.

Academic and professional background

I was educated at Boston Grammar School and scraped into medical school at the University of Nottingham in 1982 with grades AADE rather than the required BBB. I felt initially very lucky and slightly unworthy to be there but graduated uneventfully in 1987. Junior clinical posts followed in emergency medicine, anaesthesia, general medicine and infectious diseases, until I entered academic public health training in 1991, with a Certificate of Completion of Specialist Training (CCST) in 1997.

Thereafter, I was a clinical senior lecturer in public health and a consultant epidemiologist for the Public Health Laboratory Service (PHLS) until 2000. Posts in the UK pharmaceutical and vaccine industries then followed, which then culminated in my appointment as UK Medical Director for Aventis-Pasteur MSD. I rejoined the public sector in 2004 as a consultant epidemiologist at the Health Protection Agency (HPA) in Colindale, while also acting as the Head of the Pandemic Influenza Office.

Following this, I returned to Nottingham to become Professor of Health Protection in 2007. I remained there for a decade until I was seconded to the Department of Health and Social Care in 2017 as Deputy Chief Medical Officer, England. I stepped down from this role in March 2022 and have returned to the University of Nottingham as Pro Vice-Chancellor for the Faculty of Medicine and Health Sciences. This title conceals the fact that I have responsibilities across four Schools: Medicine, Health Sciences, Life Sciences, and Veterinary Medicine and Science.

> I'm one of very few doctors who can claim such a varied career … Working with Sir Chris Whitty during the SARS-CoV-2 pandemic was a huge privilege and inspiration.

Main highlights and achievements

My varied career

I think my biggest achievement is that I have been lucky enough to work in so many different organisations and workplace cultures. My career has taken me to the NHS three times – as a junior doctor, a COVID-19 vaccinator and now as a non-executive director for the NHS Lincolnshire Integrated Care Board. I have worked at three versions of a national public health authority – PHLS, HPA and Public Health England. I have also returned to the University of Nottingham in three distinct roles since my time as a student. It has been a great highlight to have worked at the World Health Organization (as a consultant and Head of a WHO Collaborating Centre on Pandemic Influenza, 2010–2017), three pharmaceutical companies and the UK government.

I've travelled to more countries with work than I could name, but Turkmenistan is the most unique. I'm one of very few doctors who can claim such a varied career. I just love working at professional interfaces – I'm basically a translator and communicator.

Along the way I've had some interesting side jobs too. I was a medical officer for Lincolnshire Army Cadet Force for 12 years and was a doctor at Donnington Park and Holme Pierrepont race venues. I was very lucky to have completed some

RETURN TO CONTENTS

Professor Sir Van-Tam speaking to the press and public at one of the government's daily COVID-19 briefings.

of my academic public health training alongside Dr Tedros Adhanom Ghebreyesus, Director General of the World Health Organization. Working with Sir Chris Whitty during the SARS-CoV-2 pandemic was a huge privilege and inspiration. My biggest mentors will always be Karl Nicholson and Richard Madeley – Karl for research; Richard for public health and political savviness.

My greatest achievements

My top achievements? I don't really know what to say. By and large, I've just turned up and tried to do each job to the very best of my ability, based on what the tasks were at the time – some were obviously quite big.

I've had a fairly solid research career. My two biggest career regrets are not having had time for more regular clinical work since 2000 and not joining the French Army in 1982, to complete my national service before medical school.

In the pathology space, the achievement highlights have to be being part of teams that have performed the world's largest and world's first human challenge studies of influenza and SARS-CoV-2 respectively and my work with the UK Vaccines Task Force (VTF). I genuinely believe the VTF and NHS COVID-19 vaccination programme have together saved tens of thousands of British lives in the last 18 months.

My military MBE in 1998 was pretty special. Being awarded The Harveian Oration (Royal College of Physicians) in 2021 was a huge honour and accolade. As were the awards of the Attenborough Lecture and medal (Royal Society) and the Thomas Francis Jr Memorial Lecture and medal (Michigan School of Public Health), which I received this year. Receiving a Knighthood in 2022 is obviously the biggest highlight of all. But, helping younger doctors and scientists with their leadership development and career progression is what really gives me a buzz, more than all the glitz. What I hope for more than anything else is that I can get to the end of my career and others will be able to say: 'he made a real difference'.

Future challenges for pathology

I'm not a proper pathologist, but a Fellow of the College by publication, so the future of pathology is hard for me to predict. However, obviously, as AI and automation rightfully become of increasing importance in the specialty, pathologists will have to adapt. I think the SARS-CoV-2 pandemic has helped us see a future where diagnostics for infectious diseases will be more important than ever before.

Maintaining work–life balance

First, take the time to find a job that's right for you or, even better, a job that you really enjoy. Then, find hobbies that you enjoy even more – try to make one of them something involving physical exertion. Finally, remember your roots, who you are ultimately here to serve, and stay grounded.

RETURN TO CONTENTS

PROFILE: DR NOHA EL SAKKA OBE

Having recently been honoured with an OBE for her services to the NHS and the COVID-19 response, Noha El Sakka shares the challenges, highlights and achievements of a career that has taken her from Alexandria to Aberdeen. She has been celebrated for her work in microbiology and virology, and was appointed as an advisor to the Scottish Government's Chief Medical Officer.

Career journey

I was born in Alexandria, Egypt and moved back there following my school years in Dubai. After receiving my MBChB, I decided to specialise in clinical pathology, obtaining a master's degree and then a medical doctorate at the Alexandria University teaching hospital.

I moved to the UK in 1999 and after obtaining my PhD in 2005 at the University of Aberdeen, undertook two years of post-doctoral research in the field of infection. I then returned to medical practice and was appointed as consultant in NHS Grampian in 2015 after completion of the FRCPath and medical microbiology training. In December 2021, I was also elected a Fellow of the Royal College of Physicians in Edinburgh.

I am delighted to have been awarded an Officer of the Most Excellent Order of the British Empire (OBE) in the Queen's Birthday Honours list in June 2022.

Key achievements

Developing a solid research skill base

Moving with my family from Egypt to the UK was particularly challenging for my career prospects. I was very keen to learn as much as possible about research methodology, new techniques and advances in the field of molecular biology and whilst working on my PhD, I attended many courses, travelling around the world for conferences and workshops. This peak learning stage provided me with a solid foundation of knowledge and skills which helped shape my future career.

Through my academic years at the University of Aberdeen, I joined eminent research groups working on infection and microbiomes under the supervision of Professor Nigel Webster, Professor Helen Galley and Professor Emad El-Omar. My research allowed me to follow the course of management of many patients with sepsis in the intensive care unit where I was fascinated by the value added to their successful outcomes by the specialty of medical microbiology. I went on to learn more about the pathogenesis of sepsis, antimicrobials and antimicrobial resistance.

> I am delighted to have been awarded an Officer of the Most Excellent Order of the British Empire...

Building a new team

I was appointed as the Director of the Microbiology and Virology service soon after my first consultant post. Shortly afterwards, I was faced with an unprecedented staffing crisis, required to preserve a service that includes microbiology, virology, infection control, training, teaching and emergency on calls in a large university teaching hospital.

In the face of adversity, I learned the valuable skills of leadership and crisis management. I learned the skills of prioritisation, recruitment policy, negotiation, horizon scanning, resource management and team working with plentiful support from my colleagues. I was privileged to work under the leadership of Dr Bernie Croal (current RCPath Chair, Scotland Regional Council and President of the Association for Clinical Biochemistry and Laboratory Medicine [ACB]), who is an exceptional leader and role model. The

RETURN TO CONTENTS

service redesign policy was successful with better understanding of different skill sets and how to deploy professional areas of expertise. I certainly feel that the emphasis on the values of team working, professionalism and efficiency help our staff to thrive, be productive and feel appreciated, with a positive and proactive attitude towards successful service provision.

> During the pandemic, I was tasked with a leading role as part of the local and national COVID-19 response.

Challenging COVID-19

I was appointed as the Virology Specialist Advisor to the Scottish Government (SG) and to the Chief Medical Officer (CMO), Professor Sir Gregor Smith in March 2018.

During the pandemic, I was tasked with a leading role as part of the local and national COVID-19 response. In particular I led on the complex diagnostics and infection control aspects of the COVID-19 response locally, including introduction and upscaling of testing, training and incident and outbreak management, as well as developing infection control guidance, clinical pathways and policies.

At a national level, I was involved in advising the SG and CMO as a subject matter expert on the clinical, diagnostic, testing, vaccination and quality aspects of the COVID-19 response including development of guidelines, clinical governance frameworks and technical development.

I led the development of the COVID-19 testing in the North Regional Hub responsible for turning around thousands of samples daily, seven days a week.

It was truly an honour to receive an OBE for my service to the NHS and the COVID-19 response in June 2022. Receiving such an acknowledgement by the UK Government and in particular by Her Majesty Queen Elizabeth II before her sad passing is an outstanding achievement that I will always treasure greatly.

The challenges that change brings

Laboratory medicine is a rapidly changing field with technology and the science behind it moving forward at a quick pace. For us to keep up to date and be part of the race, there needs to be a strategy embedded in teaching, training, research and service provision with the vision and ability to rapidly adapt to changes.

> The diverse scope of laboratory medicine allows you to develop an area of specialist interest to an expert level, [which] provides a versatile array of knowledge that makes a career in laboratory medicine very exciting.

New technologies come with new skill sets and price tags that need to be matched with funding and staff shortages representing two key challenges in the current economic environment.

RETURN TO CONTENTS

We need to investigate new models of working that can efficiently direct the available resources to the right place. The model of regional working based on the established service, skills, demands and geographical location has the potential to provide a cost-effective and efficient solution with several examples of successful models. However, this needs to be backed by the required logistics, IT, staffing, funding stream and infrastructure.

Similarly, in relation to staff shortages in laboratory medicine, it is important to explore different ways of working, without compromising standards and competencies. Training of different grades of staff to undertake particular tasks may help backfill gaps and allow other specialists to focus on areas requiring their expertise.

> One of the most exciting aspects of pathology is the breadth of healthcare covered – you provide a service to patients in medicine, surgery, adults, children, acute, community and intensive care – basically everyone.

The College provides the Medical Training Initiative scheme, which is excellent for supporting skilled international medical trainees and integrating them into the system and the staffing establishment for those seeking to work in the UK.

Clinical research needs to be more established in the field of laboratory medicine with explicitly identified routes for funding, scholarship schemes, research facilities and having a connection with academia to help establish the much-needed link between healthcare and clinical research.

The excitement of a career in pathology

One of the most exciting aspects of pathology is the breadth of healthcare covered – you provide a service to patients in medicine, surgery, adults, children, acute, community and intensive care – basically everyone. This needs multi-agency links, where you work among a multidisciplinary team and you have the chance to see the full picture and discuss your views with others involved in the patient's care. Through this, you can appreciate the added value of your specialty and professional skills in the patient's journey right from the sample on the bench or under the microscope to the delivery of clinical care at the other end.

Furthermore, the diverse scope of laboratory medicine allows you to develop an area of specialist interest to an expert level. This type of broad interaction provides a versatile array of knowledge that makes a career in laboratory medicine very exciting.

Maintaining work–life balance

All through my career, I have had amazing support from my family. Despite a busy schedule, I make time for my family and my friends while ensuring I also have some time for myself. I try to be flexible, positive and motivated. One useful tip is to resolve conflicts quickly and objectively and then move on. I travel a lot and like to explore new places and meet new people.

RETURN TO CONTENTS

FORENSIC VETERINARY PATHOLOGY

Veterinary pathologists work in animal disease surveillance, prevention, diagnosis and treatment. They investigate diseases in pets and farm animals, as well as rare and exotic species. Forensic veterinary pathology is concerned with forensic investigation of animals in criminal or legal incidents. Here, Professor John and Margaret Cooper present the key advancements and responsibilities of this burgeoning discipline.

Six decades of advancement in forensic veterinary pathology

Professor John Cooper

Margaret Cooper

In this article, veterinary pathologist Professor John Cooper, with his wife and colleague, animal lawyer Margaret – Fellow and Honorary Fellow, respectively, of the College – discuss the history and development of forensic veterinary medicine, from its beginnings as an unrecognised specialisation to its growing presence in the training and practice of pathologists.

Introduction and some personal reflections

The Royal College of Pathologists was founded on 21 June 1962, just four months before we met as fresher undergraduates at Bristol University. We were not to marry until 1969 but, during the succeeding years, we took every opportunity to amalgamate our academic training as a veterinary surgeon and a solicitor, respectively. We participated enthusiastically in activities concerning wildlife conservation and animal welfare that might benefit from a lawyer's approach as well as a veterinary input. So, we started working as a team.

John's eyes were opened to the challenges of forensic medicine because one of his lecturers was a Home Office pathologist who used human museum specimens in his lectures to veterinary students. The term 'forensic veterinary medicine' was not used in those days, even though members of the veterinary profession had long played an important role as expert witnesses in court cases concerning domesticated species.

Indeed, the expression 'to vet' – meaning to make a careful and critical examination, which originated in work with horses – is a reminder of the esteem in which a veterinary surgeon's assessment of an animal was viewed. Veterinary surgeons also were often involved in cases where a veterinary, as well as a medical, opinion was needed, such as bites and kicks from livestock.

The advent of veterinary forensic medicine

The emergence of veterinary forensic medicine as a distinct subject in Britain took place in the early 1980s and was engendered by two separate issues:

1. growing concern about animal welfare and the need for sound scientific evidence to prosecute or defend those charged with causing harm to animals
2. the expansion of legislation and law enforcement in respect of wildlife crime[1] and increasing awareness that appropriately experienced veterinary pathologists could be of great assistance in investigations and the provision of evidence.

RETURN TO CONTENTS

Figure 1. Veterinary students learn forensic post-mortem techniques from Professor Cooper, in this case on a captive *Boa constrictor* that was found dead under strange circumstances.

In contrast to the situation in human medicine, there was, at that time, no recognised route to specialisation in forensic veterinary medicine or pathology. Those involved were usually self-taught or gained a qualification based on training for work with humans or a more broadly-based course in forensic science.

Over the past two decades, the situation has improved to a certain extent. Forensic teaching has been introduced into the undergraduate programmes at certain British veterinary schools (see Figure 1). Some of the latter have established departments focusing on (especially) forensic pathology.

Newbery et al. (2016), writing in a special focus issue of *Veterinary Pathology* – itself a major contribution towards developing the scientific basis of veterinary forensic pathology – argued that the key to strengthening veterinary forensic medicine and pathology is education at the undergraduate level and, perhaps more urgently, as a postgraduate specialism.[2]

The concept is taking time to put into practice, however, and openings for formal post-graduate training remain limited. Notwithstanding this, the European College of Veterinary Pathologists, established in 1995 to advance veterinary pathology and to promote standards within the specialty in Europe, recently introduced a Certificate in Forensic Veterinary Pathology.[3]

> What, then, does veterinary forensic medicine ... comprise? Essentially, it encompasses any situation where animals are involved in criminal or other legal actions.

The College has a Specialty Advisory Committee in Veterinary Pathology but has not as yet established a specific focus for veterinary forensic practitioners. Recently, however, veterinary graduates became eligible to become Associate Members of the Faculty of Forensic & Legal Medicine of the Royal College of Physicians.

There are a few other, mainly postgraduate, often online, training opportunities in different parts of the world – for example, covering wildlife forensic pathology at the University of Florida.

Recent trends

Traditional veterinary forensic medicine and pathology originally related to domesticated animals but are gradually metamorphosing into a more broadly-based discipline.[4] This can probably better be described as either 'animal' or 'comparative' forensic medicine.[5] The former term ('animal forensics') is increasingly gaining acceptance when

Figure 2. Post-mortem examination of a beached Bryde's whale (*Balaenoptera brydei*). The tide is approaching, bad weather looms, the carcass is decomposing and the team members are tiring.

RETURN TO CONTENTS

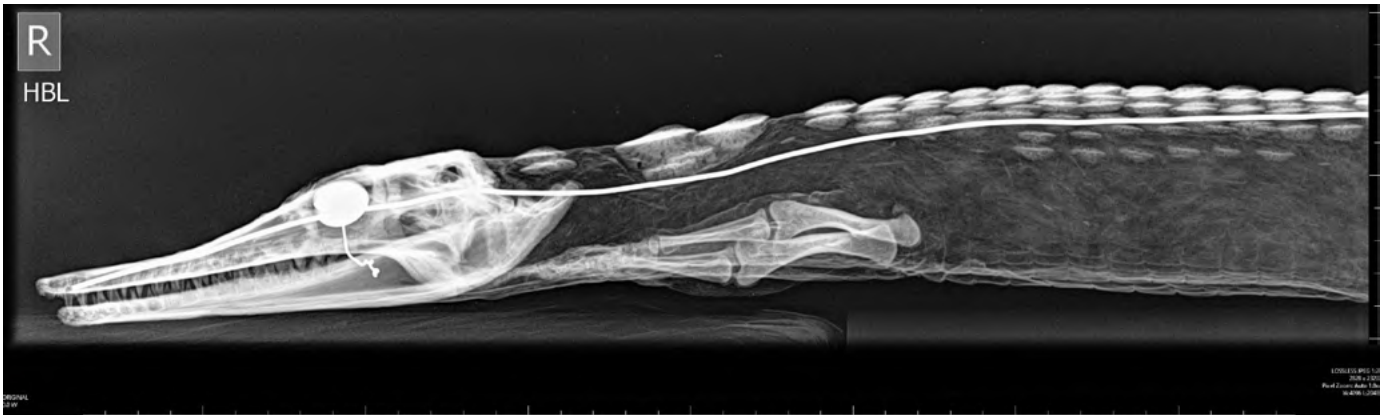


Figure 3. A radiograph of a mounted Nile crocodile (*Crocodylus niloticus*) reveals some of the materials used in its preparation and may thereby permit identification of the taxidermist.

describing scenarios in which diverse, not just domesticated, species in the Kingdom Animalia are involved.

This approach was given a boost in 2021 at the 1st International Virtual Meeting of Forensic Animal Sciences. The organisers, Dr Victor Toledo and his colleagues, proposed the adoption of the designation 'forensic animal science' for this emerging, broad-based discipline. Their argument for a change in terminology was that, although the modern veterinary profession encompasses specialists in fields ranging from anaesthesia to zoological medicine, investigation of many animal-related forensic cases requires the input, not only of veterinarians, but of other specialists such as vertebrate and invertebrate zoologists, conservationists, ethologists, nutritionists and biomedical scientists.

> Forensic studies on both domesticated species and wildlife is a relatively new, but rapidly growing, addition to the gamut of subjects that contribute to the science behind the cure.

The features of veterinary forensic medicine

What cases do they investigate?

What, then, does veterinary forensic medicine (as we shall continue to call it here) comprise?

Essentially, it encompasses any situation where animals are involved in criminal or other legal actions. The word 'forensic' refers to actions related to a court of law.

Many attributes of forensic work with animals are similar to those encountered when dealing with humans. Differences usually relate to the disparate biological characteristics of some of the species involved, ranging from dogs to dolphins and cats to crustaceans, and the diversity and unpredictability of the locations of incidents, especially when free-living animals feature.

Animals can be either the victim or the instigator of an incident. In addition, animals can serve as sentinels, or witnesses, to an occurrence or themselves be a source of evidence in the form of DNA or other derivatives.

This breakdown is described in a little more detail below.

The animal is the victim when subjected to injuries and other insults, maliciously or accidentally. There has been extensive study of some forms of human-induced damage to animals – for example, ill-treatment of working animals, non-accidental injuries caused to dogs and cats (see later) and the effects of traps, snares and firearms on wildlife.

The animal is the instigator when domestic or wild species give rise to injuries, such as bites, trauma, electrocution, envenomation and hypersensitivity reactions, transmit infections or damage property.

What techniques are used?

What characterises investigative techniques in animal cases? First and foremost, the wide range of animal species with which a clinician or pathologist deals means that no one technique is likely to be applicable to all. For example, post-mortem examination of a tortoise requires a different approach from that for a tapir or a tarantula spider. Very large species may necessitate a team effort (Figure 2).

By contrast, small species such as amphibians, fish and invertebrates and diminutive specimens such as embryos, eggs and fetuses, are likely to require micro-techniques, such as the 'mini-necropsy'.

> Animal bites are a common example of where forensic investigations may benefit from medical, dental and veterinary cooperation.

Laboratory investigations on forensic samples from live and dead animals are generally similar to those employed in human forensic medicine, but there are some differences. The temperatures used to incubate cultures can differ, either because some species are cold-blooded (ectothermic) or because warm-blooded (endothermic) taxa have different body temperatures.

RETURN TO CONTENTS

Figure 4. A newborn lamb that may have died of natural causes or as a result of a dog harassing the ewe. The dead lamb may also have been scavenged.

Veterinary pathologists may have to exercise ingenuity on occasion – for instance, if asked to assist in ascertaining the species and likely provenance of prepared specimens (taxidermy), trophies and egg collections (Figure 3). They may also identify body parts, particularly when they are believed to be of animal origin.

> It has given us pleasure to have been able to play a small part in the evolution and metamorphosis of veterinary forensic medicine...

The crime scene in animal forensic work may range from a wounded dog in a suburban bungalow or a dead lamb on a farm (Figure 4), to a beached dolphin or a poached elephant carcass in the African bush. Suspected cases of wildlife crime are often in isolated locations, with few facilities for proper investigation and a paucity or absence of police, enforcement officials or crime scene specialists. Investigation under such conditions can be both difficult and dangerous. Evidence may be disturbed by wild animals or by wind, rain or snow. The risk of disease, such as anthrax or Ebola, may mean that an investigation or a full post-mortem examination cannot be undertaken.

Veterinary–medical collaboration

Those carrying out forensic pathology investigations on animals may need to work with their colleagues in human forensic work. At present, this is most likely in cases where there are both animal and human elements, such as dog bites, cattle trampling incidents and zoonotic infections. Sometimes a legal case may require the post-mortem investigation of both the cadaver of a dead person and the carcass of a dead animal – for instance, because an assailant has shot or poisoned both a householder and their pet dog.

Animal bites are a common example of where forensic investigations may benefit from medical, dental and veterinary cooperation.

Links between abuse of humans and violence to animals are increasingly attracting attention and study. The College has played a part in raising awareness. In 2011, it hosted a landmark Symposium on the Pathology of Abuse in Animals and Humans, organised by Richard Shepherd and John Cooper. This event was attended by physicians, paediatricians, veterinary surgeons, pathologists, animal welfarists, social workers and police officers.

Evolving veterinary forensics

It has given us pleasure to have been able to play a small part in the evolution and metamorphosis of veterinary forensic medicine and to see the strides that are being made to broaden its remit and to provide training for young colleagues.

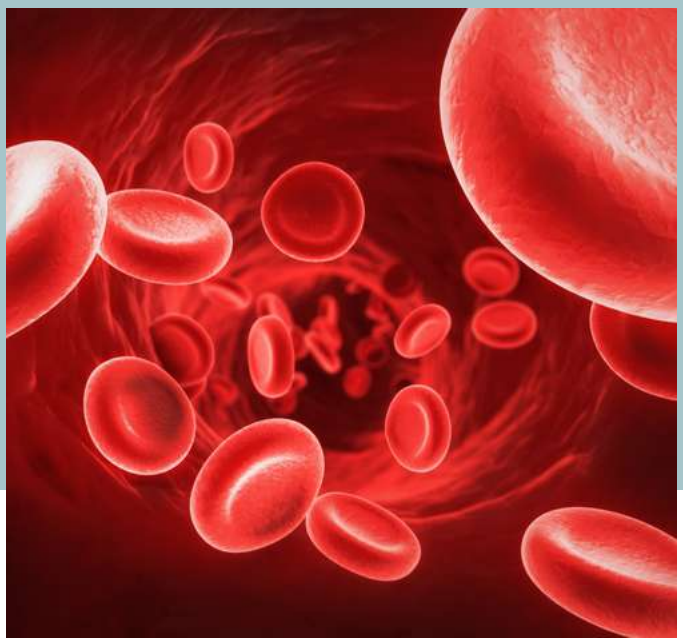
When the College was founded six decades ago, its aim was to develop and support the various evolving specialties of pathology. From the outset, the College welcomed members of the veterinary profession into its ranks. Previous articles in the *Bulletin* in this Jubilee year by Professor Roberto La Ragione and Lucy Oldroyd and colleagues have illustrated that this confidence in veterinary pathologists was not misplaced. Forensic studies on both domesticated species and wildlife is a relatively new, but rapidly growing, addition to the gamut of subjects that contribute to the science behind the cure.

References available on our website.

Professor John E Cooper
Specialist in Veterinary Pathology
Diplomate, European College of Veterinary Pathologists
Diplomate, European College of Zoological Medicine

Mrs Margaret E Cooper
Solicitor (not in private practice)
Wildlife Health, Forensic and Comparative Pathology Services (UK)

RETURN TO CONTENTS



Haematologists are experts in blood cells, including those circulating around the body and in the blood cell factories of the bone marrow. Haematologists diagnose and treat malignancies such as leukaemia and anaemias like sickle cell disease. They also deal with abnormalities of the blood clotting system, such as haemophilia. This section features an introduction to the history of chronic myeloid leukaemia and an exploration of novel therapies for thrombotic thrombocytopenic purpura.

Chronic myeloid leukaemia: a paradigm shift in diagnosis and treatment

Harry Robertson

Jane Apperley

Harry Robertson and Jane Apperley introduce the story of chronic myeloid leukaemia, with a history that stands as an exemplar for the remarkable advances that can be achieved through close collaboration between pathologists, clinicians and the pharmaceutical industry.

Chronic myeloid leukaemia (CML) was once a uniformly fatal disease. However, this illness is now typically a chronic, and even on occasion curable, condition. Many of the seminal moments driving this change are rooted in British medical science.

The history of CML

Early identification of the disease

The first description of CML is traditionally attributed to one or other of Rudolf Virchow or John Hughes-Bennett, who described 'white blood' in 1845. Virchow later gave credit for the first description to Hughes-Bennett.

In fact, David Craigie, the physician who looked after two cases of presumed CML in Edinburgh and made the connection that he was observing the same disease, published his findings in the same edition of the Edinburgh Medical and Surgical Journal as Hughes-Bennett, the pathologist who performed the autopsy on the second case.

CML had probably been described earlier in 1825 in France by Velpeau, and in 1839 by Alfred Donne, a distinguished French microscopist under whom Hughes-Bennett had trained.[1] Sir Arthur Conan Doyle described the first treatment of CML in 1882, using Fowler's solution (containing arsenic) to control the white cell count.[2]

A major breakthrough came in 1960, when Nowell and Hungerford described a minute chromosome in seven cases of the disease known as chronic granulocytic leukaemia.[3] In fact, the same abnormality was discovered the same year in Edinburgh, where the first description was generously attributed to their US colleagues, hence the name Philadelphia (Ph+) chromosome.[4] Janet Rowley (Chicago) described the reciprocal translocation between chromosomes nine and 22 in 1973.[5]

> Many of the seminal moments driving this change are rooted in British medical science.

Development of treatments

In 1969, John Dacie, Chair of the first UK department of academic haematology at the Royal

RETURN TO CONTENTS

Postgraduate Medical School (RPMS), hosted the MRC Leukaemia Unit, with David Galton as the first director. Galton conducted the first randomised study in CML, busulphan vs splenic irradiation, where he demonstrated a survival advantage for chemotherapy.[6]

Busulphan was superseded by hydroxycarbamide and then by interferon (IFN). The use of IFN (beginning in China) became widespread following the work of Moshe Talpaz, who described the partial or complete loss of Ph+ metaphases from bone marrow-derived karyotypes. The CML subgroup of the MRC Working Party published their randomised study of IFN vs busulphan/hydroxycarbamide in 1995, demonstrating a survival advantage for IFN irrespective of cytogenetic response.[7]

> A major breakthrough came in 1960, when Nowell and Hungerford described a minute chromosome in seven cases of the disease known as chronic granulocytic leukaemia...

In 1974, researchers in Seattle reported autologous transplant in advanced phase CML using cryopreserved bone marrow-derived progenitor cells.[8] At the RPMS, John Goldman, Ray Lowenthal, Sandy Spiers and David Galton reported circulating progenitor cells in the peripheral blood of newly diagnosed patients with CML. They found the cells could be removed by leukapheresis, cryopreserved and subsequently used to autograft patients with advanced phase disease.[9]

In 1987, they described Ph+ negative haemopoiesis after autologous transplant in chronic phase, which became a popular treatment option for patients ineligible for allogeneic transplantation.[10]

In 1979, Alex Fefer, working with Don Thomas in Seattle, described four successful syngeneic transplants.[11] The patients were earlier presented at international meetings, allowing John Goldman to perform the first UK syngeneic transplant for CML at the RPMS in July 1979. This was followed by the first UK allogeneic sibling transplant in 1981, and the first unrelated volunteer donor transplant in 1985, all at the RPMS.

In 1982, Herman Waldmann, Geoff Hale and Mike Clark developed rat monoclonal antibodies capable of lysing human T-cells ex vivo through the recognition of the pan-T-cell marker, CD52, and complement activation. They suggested their use in allogeneic transplants (allo-SCT) to reduce the incidence of graft versus host disease (GvHD).[12] Although the technology was highly effective in ameliorating GvHD, it resulted in an increased risk of relapse confirming the existence of the graft versus leukaemia (GvL) effect.[13]

In 1982, John Groffen, Gerard Grosveld, Nora Heisterkamp, Anne Hagemeijer, Claus Bartram and colleagues reported that the viral oncogene c-abl moved from chromosome 9 to chromosome 22 and subsequently identified the breakpoint regions on chromosome 22.[14–16]

The following year, Eli Canaani and colleagues described the BCR:ABL1 fusion gene, soon followed by the characterisation of the fusion protein, a dysregulated tyrosine kinase, by the group of David Baltimore.[17,18] The final piece of the jigsaw was added by George Daley, Rick van Etten and David Baltimore in 1990, when they reported that aberrant expression of BCR:ABL1 could induce a CML-like disease in mice.[19]

Current CML outlook

Modern testing and treatments

By this time, CML was the most frequent indication for allo-SCT. In 1990, Hans Kolb (Munich), effectively used infusions of lymphocytes from the original donors (DLI), to treat patients relapsing after transplant,[20] a technology further optimised by Steve McKinnon and Francesco Dazzi.[21,22]

Safety and efficacy were improved by using escalating doses of DLI as early as possible after identification of relapse. This highlighted the need for a sensitive test for disease recurrence and was facilitated by the development by the PCR test by Kary Mullis in 1987.

Work at the RPMS over the next decade – commenced by Gareth Morgan, improved by Tim Hughes and optimised by Nick Cross – resulted in a quantitative reverse transcriptase PCR assay (RT-qPCR) that not only detected BCR:ABL1 transcripts but indicated whether they were decreasing over time as a result of the GvL effect, or increasing and necessitating DLI.[23,24]

In the 1990s, the BCR:ABL1 protein was crystallised. Elizabeth Buchdunger, Jorg Zimmerdam and Nicholas Lydon at Ciba-Geigy developed phenylaminopyrimidine inhibitors of the Abl kinase domain.[25] These were tested against malignant cell lines by Brian Druker, then a clinical fellow at the Dana Faber Cancer Center (Boston), which were found to be selective for cell lines derived from patients with CML.[26]

> The remarkable efficacy of TKI has restored the life expectancy of most patients to that of the normal population.

The impact of tyrosine kinase inhibitors

This led to the rapid development of an orally available drug, STI571, known as a tyrosine kinase inhibitor (TKI), and the start of a series of clinical trials in CML and Ph+ ALL. The Phase I study in advanced phase disease or IFN-resistant chronic

RETURN TO CONTENTS

phase was presented at the 1999 ASH meeting in New Orleans to a packed room.[27]

Phase II studies started in early 2000, with strong encouragement from John Goldman (as detailed in Daniel Vasella's *Magic Cancer Bullet: How a Tiny Orange Pill May Rewrite Medical History*),[28] which led Novartis to pursue licensing of STI571, now known as imatinib (Glivec), in 2001.

In 1998, as Brian Druker was treating the first patients with STI571, Alois Gratwohl, Jane Apperley and European Group for Blood and Marrow Transplantation (EBMT) colleagues published the Gratwohl/EBMT score, which used five pre-transplant parameters (age, disease phase, time from diagnosis to transplant, donor type and sex match of donor and recipient) to predict the outcome of transplants in CML.[29] The number of transplants performed annually for CML peaked in 1999 and declined dramatically thereafter as imatinib became clinically available – but long before the demonstration of durable responses.

> The results of the Destiny study are the most promising, with almost 70% of patients remaining off-drug, a remarkable achievement for a previously incurable disease.

Further advances in tyrosine kinase treatments

In 2002, Mercedes Gorre, working with Charles Sawyers, found that some patients became imatinib-resistant through point mutations in the kinase domain.[30] Since then, almost 100 mutations have been described, resulting in the development of additional TKIs – most recently ponatinib, the only licensed TKI with efficacy against the T351I mutation, and asciminib.

Centres in the UK (Hammersmith & Kings in London, Glasgow, Leeds, Liverpool, Newcastle, Nottingham and Oxford) participated in seminal trials that led to the licensing of all six TKIs. In 2002, Jane Apperley and colleagues demonstrated the efficacy of imatinib against clonal eosinophilic disorders characterised by aberrations of platelet-derived growth factor receptor (PDGFR) and PDGRF beta.[31]

UK colleagues were represented in the European LeukemiaNet (ELN) international consensus group's highly cited guidelines for CML management (2006, 2009, 2013, 2020).[32] Notable UK contributions include: John Goldman and Nick Cross's efforts to establish an international scale for reporting RT-qPCR results; Junia Melo identifying other mechanisms for TKI-resistance; the Hammersmith's observations of the importance of early molecular responses; the impact of non-compliance and biomarkers of prognosis at diagnosis; Hugues de Lavallade's development of next generation sequencing for mutation detection; and Jane Apperley's work in defining safe practice for parenting.

During her post-doc in Vancouver with Alan and Connie Eaves, Tessa Holyoake discovered that more than 50% of single primitive stem cells out of cycle were Ph+ and returned to Glasgow to explore ways of targeting leukaemic stem cells.[33] Imatinib sensitive, patient-derived CD34+ cells were stimulated to proliferate and differentiate. The addition of imatinib eradicated dividing cells, leaving only the quiescent fraction.

Mhairi Copland reported similar results using the second generation TKI, dasatinib. Holyoake, Copland, David Vetrie and Tony Whetton took a systems neology approach to identify novel approaches to eradicate CML stem cells, culminating in the identification of EZH2, and the combination of upregulation of p53 and downregulation of c-Myc as potential therapeutic strategies.[34]

The remarkable efficacy of TKI has restored the life expectancy of most patients to that of the normal population. Long-term clinical trial outcomes report 10-year survival rates greater than 80% with the most common cause of death being unrelated to CML. Many groups have studied treatment discontinuation and found that up to 50% of patients with deep and durable responses to TKI can cease treatment indefinitely.

In 2019, Richard Clark, on behalf of the National Cancer Research Institute's CML subgroup, published a conceptually unique study in which patients with deep molecular responses were first de-escalated to 50% of the standard dose for 12 months before stopping their TKI. The results of the Destiny study are the most promising, with almost 70% of patients remaining off-drug,[35] a remarkable achievement for a previously incurable disease.

Acknowledgements

The authors acknowledge the support of the National Institute of Health Research (NIHR) Imperial Biomedical Research Centre.

Disclosures

Jane Apperley has research funding from Incyte and Pfizer, is in the Speakers Bureau and is an Advisory Board Member for Incyte and Novartis.

References available on our website.

Harry Robertson
Clinical Fellow
Imperial College Healthcare NHS Trust

Jane F Apperley
NIHR Emeritus Senior Investigator
Imperial College London

RETURN TO CONTENTS

Thrombotic thrombocytopenic purpura: past, present and future

Marie Scully

John-Paul Westwood

Thrombotic thrombocytopenic purpura is a rare disorder associated with microvascular thrombi. Here, Marie Scully and John-Paul Westwood describe progress in understanding the pathophysiology supporting prompt diagnosis and the development of novel therapies towards improving patient outcomes.

Thrombotic thrombocytopenic purpura (TTP) was first described in 1924 by Moschcowitz,[1] who presented a fatal case of TTP associated with multi-organ failure over two weeks. Professors Upshaw (1978)[2] and Schulman (1960)[3] separately described cases we now recognise as congenital TTP, suggesting a deficiency in plasma and response to plasma infusion.

In 1982, Professor Moake[4] identified the presence of ultra large von Willebrand Factor (VWF) multimers, specific to TTP. In 1997–1998, Professors Furlan[5] and Tsai[6] confirmed the absence of a protein in the plasma, named VWF-cleaving protease in acute and chronic relapsing TTP cases. In 2001, Professor Gallia Levy confirmed this protein was a metalloprotease named ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) (Figure 1).[7]

40-years-old, but it can present in young children or the elderly. The incidence is estimated as one to two per million per year with a prevalence of ten per million.[8] Confirmation of the diagnosis is the demonstration of a severe deficiency of the enzyme, ADAMTS13 (less than 10%).

ADAMTS13 is important in the cleavage in the A2 region of VWF as it is secreted from endothelial cells. This physiological action generates more haemostatically active VWF multimers. VWF multimers bind with platelets and this action is important in primary haemostasis. However, in TTP, the lack of ADAMTS13 generates an increase in ultra large VWF multimers that promote increased platelet binding and aggregation. These break off as microthrombi and result in organ damage (Figure 2).

TTP is subclassified into immune mediated TTP (iTTP, 90% of cases), associated with antibodies to

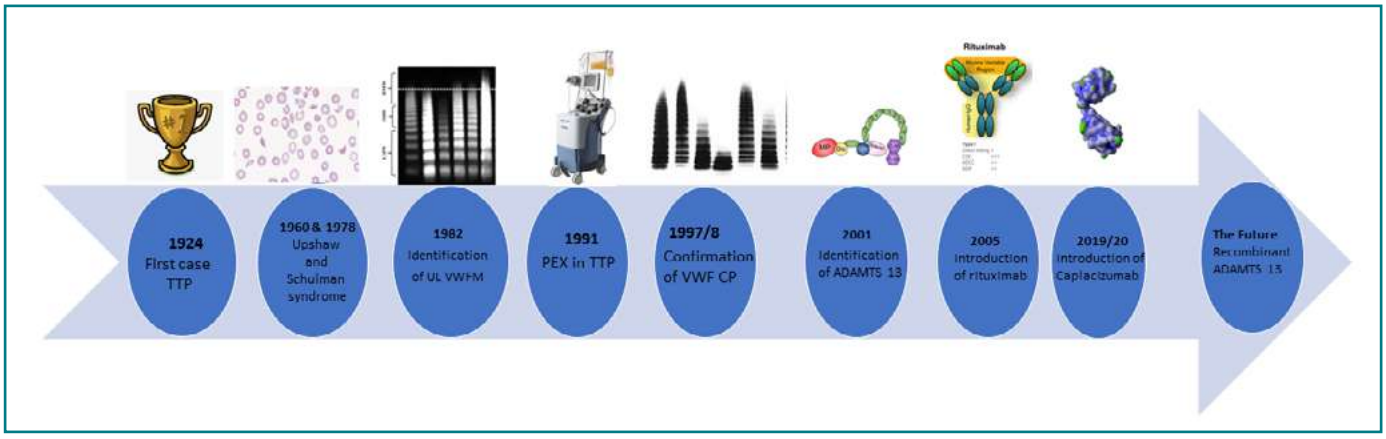


Figure 1. Main historic time points of TTP. PEX: Plasma exchange; ULVWFM: Ultra large von Willebrand factor multimers; VWFCP: von Willebrand factor cleaving protease.

Diagnosis

Central to the diagnosis of TTP is the presence of thrombocytopenia, a haemolytic anaemia with specific blood film changes, specifically schistocytes or fragmented red cells. The condition is an acute, life-threatening medical emergency, and symptoms relate to microvascular thrombi with associated end organ damage. Timing of diagnosis and treatment is critical and the heterogenous presentation may make this challenging. However, new thrombocytopenia requires a blood film analysis.

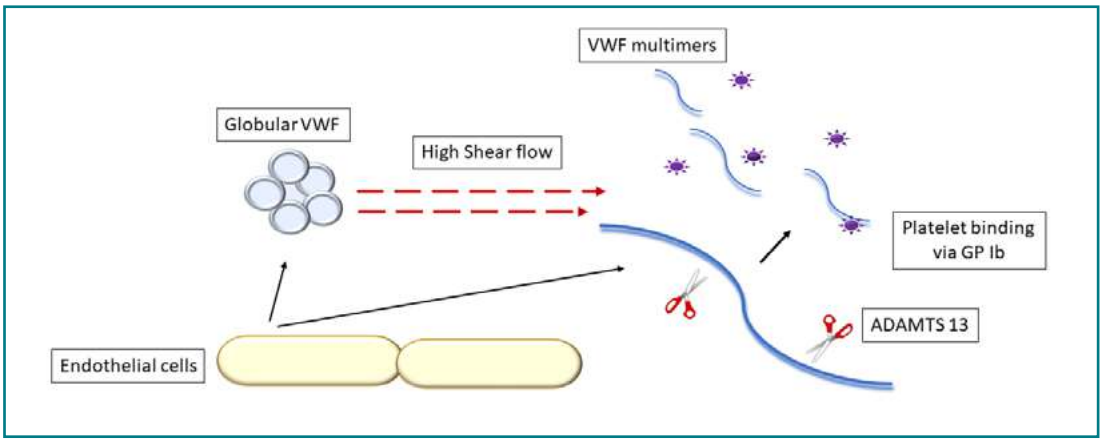
TTP occurs in women in approximately 70% of cases and the median age of presentation is

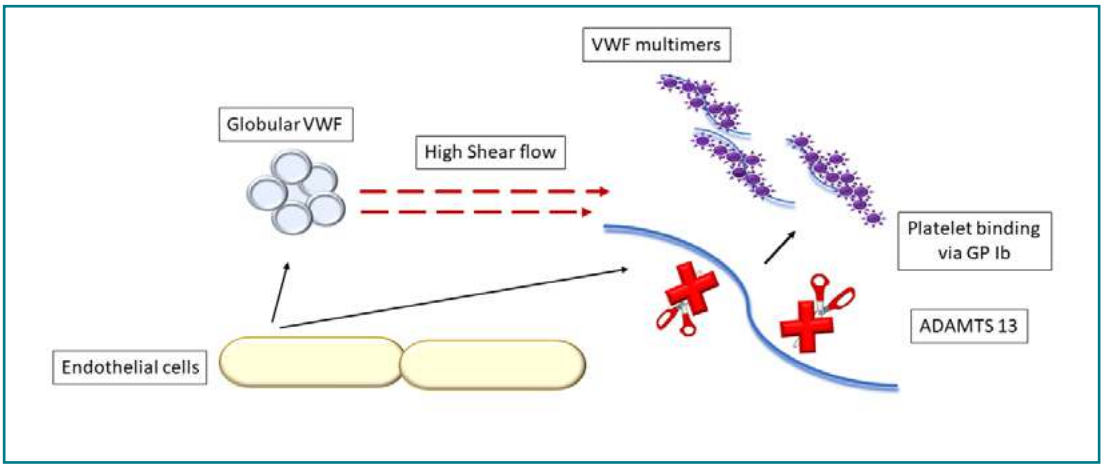
ADAMTS13, and congenital TTP (cTTP, approximately 5% of cases), caused by mutations within the ADAMTS13 gene, inherited in an autosomal recessive manner. In the remaining cases, there is a precipitating cause related to iTTP, such as pregnancy, HIV or drugs.

The past

Untreated, the mortality of TTP is over 90%. The mainstay of treatment is plasma exchange (PEX) which allows a large volume delivery of ADAMTS13. Indeed, its benefit was shown by the Canadian Apheresis Group study comparing PEX to plasma infusion (PI) in 1991.[9] This demonstrated

RETURN TO CONTENTS





(Right) Figure 2a. Normal physiological scenario: VWF and ADAMTS 13.[10]

(Below) Figure 2b. Pathological scenario: Excess platelet binding to VWF, if ADAMTS 13 prevented from acting by IgG autoantibodies.[10] VWF: von Willebrand factor.

the survival benefit of PEX to 80%. However, there remained significant morbidity and relapses.

> Pathology has been central to the progress of TTP management, particularly in the UK, via the work of clinical haematologists, laboratory biomedical scientists, specialist haemostasis laboratories and multicentre national research.

Steroids have been used since the 1980s to positive benefit in patient survival when used in conjunction with PEX, but they do not reduce relapse rates. A number of other immunosuppressive therapies were used, often associated with toxicity. The introduction of rituximab, the anti-CD20 monoclonal antibody, in the mid-2000s was the next therapeutic turning point in TTP care. Following a regimen comparable to that used in lymphoma treatment, rituximab use in acute refractory and relapsing TTP demonstrated clearance of anti-ADAMTS13 IgG antibodies and normalisation of ADAMTS13 activity levels. Earlier use of rituximab in the acute treatment pathway (within three days of admission) reduced inpatient stay to a median of 14 days (21 days if admitted to the intensive care unit). Furthermore, the time to subsequent relapse was reduced from 50% within 18 months to 15%.

The utility of rituximab in normalising ADAMTS13 activity levels has resulted in it being used to prevent TTP relapses. Monitoring of ADAMTS13 activity levels, and administration of rituximab when ADAMTS13 activity is reduced to 15–20% from normal, prevents acute TTP relapses.[10]

The present

Since 2019, following publication of the phase III international multicentre trial,[11] the nanobody caplacizumab has been used as standard of care in the acute TTP pathway in the UK. Caplacizumab is an anti-VWF antibody and binds to the A1 region of VWF, specifically on the platelet binding receptors. When given to patients with acute TTP, this results in a quicker time to platelet normalisation, which is sustained, preventing exacerbations and refractory disease. Caplacizumab does not affect the underlying ADAMTS13 axis, but is an important adjunct therapy, thereby protecting patients and maintaining clinical remission pending response to immunosuppressive therapy. Addition of caplacizumab has reduced further length of inpatient admission and, if used promptly, there is a reduction in mortality and morbidity. Although caplacizumab action on VWF results in a severe von Willebrand disease state, clinically significant bleeding is rare given the prothrombotic nature of TTP.

RETURN TO CONTENTS

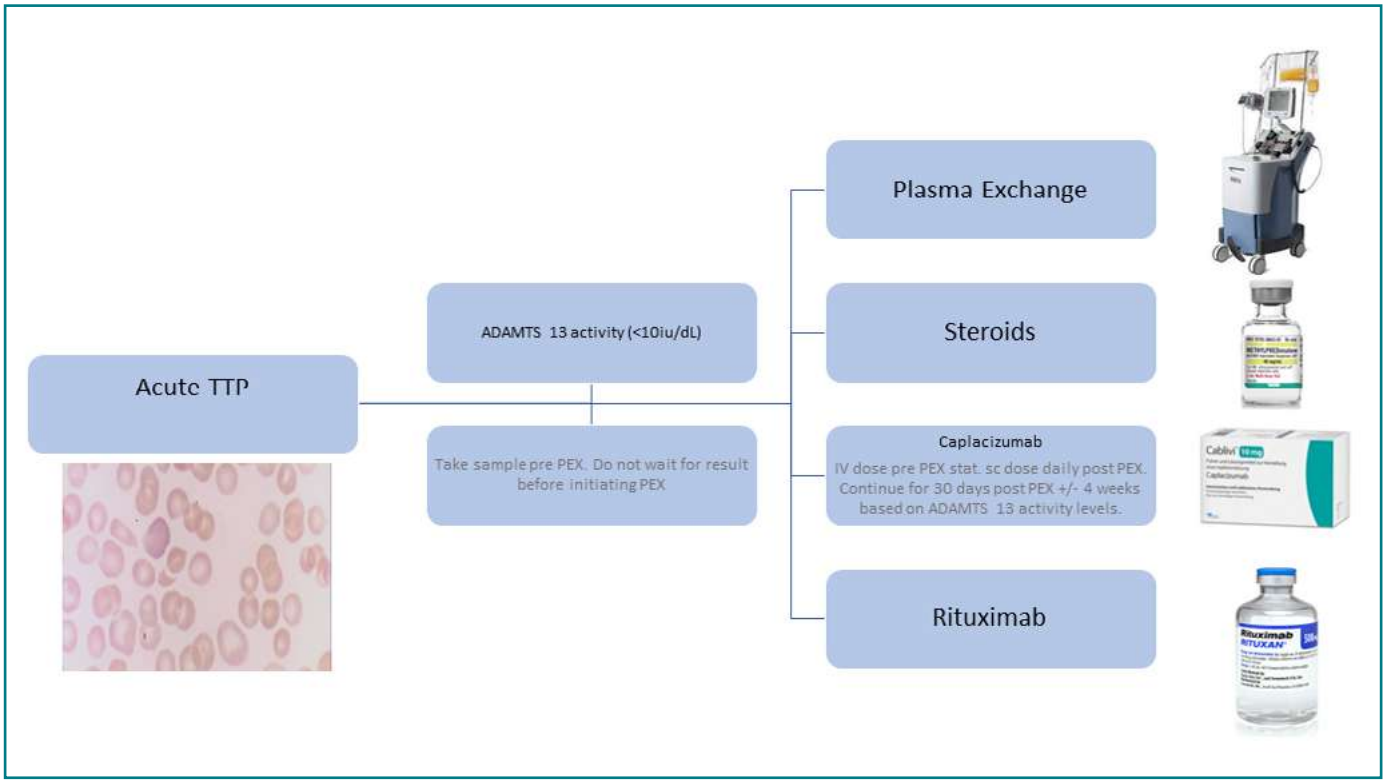


Figure 3: Summary of treatment in acute TTP.[10]

Reprinted from *Blood Reviews*, 55, M Subhan & M Scully, Advances in the management of TTP, 100945, © Elsevier, 2022, with permission from Elsevier.

The current treatment pathway in acute TTP is prompt transfer to the regional TTP centre and initiation of PEX, preferably within 4 hours whenever TTP is suspected clinically.[12] Confirmation of TTP diagnosis via ADAMTS13 activity assay should be made within 24 hours, but this should not delay treatment.

PEX is undertaken using Octaplas (Octapharma, Austria), a double viral inactivated fresh frozen plasma (FFP) with a prion reduction step. Its benefit over standard FFP relates to pathogen reduction and very low rates of reactions, a significant factor when the median volume of plasma in an acute TTP episode is 40 litres. Other key components of acute therapy are immunosuppression with steroids and rituximab, and early use of caplacizumab (Figure 3).

The incidence of cTTP is less than one per million per year. It is now clear that most cases occur in adults, mainly women in pregnancy, and without treatment it is associated with fetal loss. Management in subsequent pregnancies is with ADAMTS13 replacement, currently with plasma infusion throughout pregnancy and the postpartum period. Indeed, the emphasis is now to treat all cTTP patients from diagnosis to prevent end organ damage (the risk of stroke in those over 40-years-old and not on treatment is 50%[13]).

Even with therapy maintaining the platelet count in the normal range, patients with cTTP may suffer symptoms; these include prolonged headaches/migraines, abdominal pain or severe lethargy. Increasing the frequency of ADAMTS13 replacement can reduce or ameliorate these symptoms.

The role of pathology

TTP requires a multidisciplinary team approach to care. Pathology has been central to the progress of TTP management, particularly in the UK, via the work of clinical haematologists, laboratory biomedical scientists, specialist haemostasis laboratories and multicentre national research.

The future

TTP is designated a highly specialised service and commissioned at a regional level within England to provide dedicated care in appointed units. This will provide equity of care, long-term follow-up and standardised treatment approaches, aiming to reduce mortality to less than 10% and relapse rates to under 15%. The future availability of the missing ADAMTS13 protein in a recombinant form will allow personalised treatment approaches for cTTP cases and ultimately avoid the need for PEX in iTTP.

References available on our website.

Marie Scully
Professor of Haemostasis and Thrombosis

John-Paul Westwood
Consultant in Haemostasis and Thrombosis
University College London Hospitals

National Institute for Health Research Cardiometabolic Programme, University College London Hospitals/University College London Cardiovascular Biomedical Research Centre, London, UK

RETURN TO CONTENTS

Transfusion doctors and scientists are haematologists who specialise in transfusion medicine. They oversee the health and wellbeing of donors, the testing of blood for infections, the management of hospital blood stocks and promotion of the safe and appropriate clinical use of blood and components. Here, Susan Brunskill and Lise Estcourt mark 20 years of success in the UK Blood Service's Systematic Review Initiative in transfusion medicine.

Twenty years of the UK Blood Service's Systematic Review Initiative

Susan J Brunskill

Lise J Estcourt

Susan Brunskill and Lise Estcourt celebrate 20 years of the Systematic Review Initiative in transfusion medicine. In this article, they highlight the programme's critical role in reviewing clinical practice, spearheading scientific research and updating transfusion safety standards.

Origins of the Systematic Review Initiative

This year marks the 20th anniversary of the Systematic Review Initiative (SRI) in transfusion medicine. The SRI was created following a call by the NHS Executive in their Health Service Circular 'Better Blood Transfusion'[1] to develop the evidence base in the field of blood transfusion. Professors Mike Murphy, David Roberts and Brian McClelland answered this call and, with funding from the UK Blood Services, established the SRI in 2002.

In October 2002, with expert methodological support from Professor Chris Hyde, a clinical research fellow and a junior systematic reviewer joined the SRI and began to explore how to address the SRI's objective of increasing the evidence base for the practice of transfusion medicine. We began addressing this by undertaking and publishing systematic reviews, and, since 2003, through the development of our evidence libraries: www.transfusionevidencelibrary.com and www.stemcellevidence.com.

The Systematic Review Initiative in 2022

The SRI has grown substantially in the last 20 years; the original clinical research fellow and junior systematic reviewer remain an integral part of the team as a principal investigator and SRI manager, respectively. The current team comprises three systematic reviewers, three information specialists, a manager and three principal investigators. Professor Lise Estcourt succeeded Professor Mike Murphy as director in November 2021.

The SRI is supported by an independent steering committee consisting of representatives from relevant professional bodies and clinical experts from the UK, France, Australia and North America. Over the years, we have welcomed many clinical fellows to the team who have completed transfusion medicine systematic reviews as part of their research studies; many have continued with their research as they have moved to senior clinical roles in UK and international health services.

Our systematic reviews

Our first systematic review, published in 2004, explored whether fresh frozen plasma was clinically effective.[2] Since this first review, we have answered more than 70 systematic review questions and published over 240 articles in peer-reviewed scientific journals. Our reviews have covered the whole

RETURN TO CONTENTS

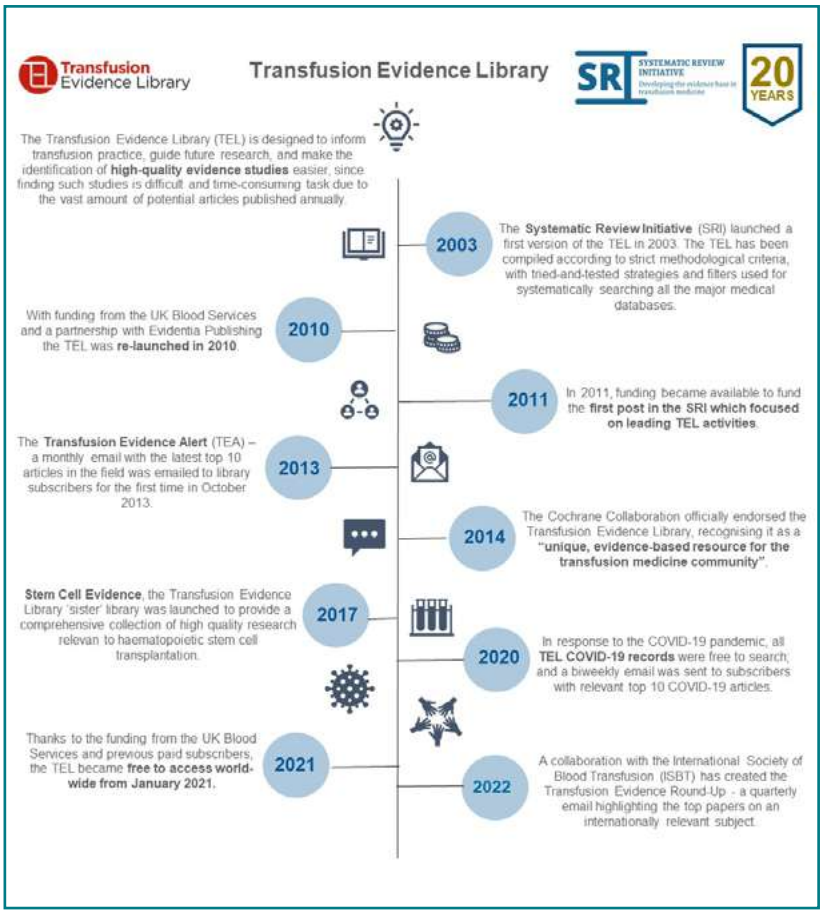


Figure 1. Milestones in the history of the Transfusion Evidence Library.

spectrum of transfusion medicine, although much of our recent focus has been on reviews that address the optimisation of blood component usage and interventions used as alternatives to transfusion.

We have been recipients of two National Institute for Health Research programme grants in the past eight years. The first focused on the safe and appropriate use of blood components and saw the completion of over 20 single intervention reviews in three years. The second used a complex statistical methodology, network meta-analysis, to compare in a single review many alternatives and adjuncts to transfusion to prevent and treat bleeding in people who are at risk of serious or life-threatening bleeding. These reviews in four clinical areas – cardiac, vascular surgery, trauma medicine and surgery, and elective orthopaedic surgery – will be published in the Cochrane Library through the course of 2022–2023.

Decisions on what systematic reviews to undertake and support in transfusion are made according to our priority checklist. This checklist is informed by a James Lind Alliance priority setting partnership we undertook between 2016 and 2018.[3]

The impact of our systematic reviews

The number of publications alone cannot be used to demonstrate the impact of research activities. Therefore, annually, we measure our impact on clinical practice, informing further research and influencing policy. In the last year, our systematic reviews have influenced 36 guidelines. In the last five years, we have influenced over 100 guidelines, including those published by the World Health Organization, the British Society of Haematology and the European Society of Anaesthesiology.

Case studies

An interesting and informative way to consider the impact of any research is to understand its story. Very often, our systematic reviews form part of a story of a clinical trial or a change in practice. Three such examples are presented here.

Supported change in blood donation guidelines

In the UK in 2007, existing blood donors who developed non-insulin-dependent diabetes (NIDDM) or who were treated for hypertension were unable to donate blood, due to concerns for any detriment to their or a potential recipient's health. Potential new donors were also not eligible to donate if they had either condition. However, such ineligibility to donate was considered a potential threat to the future sufficiency of the blood supply.[4] We were commissioned, as part of a wider project on re-evaluating UK blood donor exclusion criteria, to conduct a systematic review of the evidence for excluding donors with treated hypertension and NIDDM controlled by oral hypoglycaemic drugs.

> Decisions on what systematic reviews to undertake and support in transfusion are made according to our priority checklist.

The review identified 16 relevant papers. Although none directly addressed the review questions, all included papers provided contributory data and the findings were consistent. No study found any evidence of increased risk to blood donors with treated hypertension or raised systolic blood pressure up to 200 mmHg. We found very limited data relating to blood donation by diabetic subjects. This review supported changes to blood donor guidelines, which were implemented in 2008.

Risk of side effects highlighted over multiple updates

Cochrane reviews are updated at regular intervals. This process of adding new data to existing analyses can reveal interesting patterns in outcome data that would not be observed outside of such a setting. One example is our review of recombinant factor VIIa (rFVIIa) for the prevention and treatment of bleeding in patients without haemophilia (updated four times between 2007 to 2012).[5]

RETURN TO CONTENTS

The benefits and risks of off-label use of rFVIIa in patients without haemophilia were contested.

At the latest update, our review contained 29 trials: 16 assessed prophylactic use of rFVIIa (1361 participants) and 13 assessed therapeutic use of rFVIIa (2,929 participants). There were mixed results in terms of the benefit (mortality, blood loss, use of red blood cell transfusion) of rFVIIa when compared to placebo. However, evidence for the risk of arterial events had increased over the three versions of the review and led to the conclusion in 2012 that 'the results indicate increased risk of arterial events in patients receiving recombinant FVIIa. The use of recombinant FVIIa outside its current licensed indications should be restricted to clinical trials'.[5]

> Since this first review, we have answered more than 70 systematic review questions and published over 240 articles in peer-reviewed scientific journals.

From review to a clinical trial

Our systematic review on the use of platelet transfusions for the prevention of thrombocytopenic bleeding was first published in 2004 and has been updated multiple times.[6] The premise for this review was, while the ready availability of platelet concentrates to treat bleeding had been life-saving, there was still much debate about the use of prophylactic platelet transfusions to prevent thrombocytopenic bleeding.

The original review concluded that there was no reason to change clinical practice based on the evidence available. However, the unresolved uncertainty prompted one of the review authors to consider what further research could be undertaken to address the question about the use of prophylactic platelets. Working with other colleagues in NHS Blood and Transplant, the trial of prophylactic platelets study compared patients receiving platelet prophylaxis with those who did not. The trial, published in the New England Journal of Medicine in 2013,[7] supported the need for the continued use of platelet prophylaxis in patients with a haematological malignancy for reducing bleeding as compared to no prophylaxis.

The Transfusion Evidence Library

This year is also a milestone year for one of our evidence libraries, the Transfusion Evidence Library (Figure 1). It is 10 years since we formed a partnership with the digital publisher, Evidentia Publishing. Together, we strive to achieve the aims of the Transfusion Evidence Library, which are to inform transfusion practice, guide future research and provide easy access to high-quality evidence studies.

The Transfusion Evidence Library is a database of systematic reviews and randomised controlled trials relevant to transfusion medicine. It is fully searchable, updated monthly and aims to be a key resource for medical practitioners, policymakers and researchers both in the UK and around the world.

It has a wide scope including donation practice, use of blood components, transfusion alternatives and the management of anaemia. The Transfusion Evidence Library is supported by a monthly evidence alert. The evidence alert highlights the top ten most recent papers added to the Transfusion Evidence Library in the last month and is sent to over 9,000 email addresses.

In 2014, the Cochrane Collaboration officially endorsed the Transfusion Evidence Library, recognising it as a 'unique, evidence-based resource for the transfusion medicine community'. Last year we began a collaboration with the International Society of Blood Transfusion (ISBT) to create the new, quarterly Transfusion Evidence Round-Up. This highlights high-quality evidence studies, selected by ISBT members, about an internationally relevant subject in the field of transfusion medicine.

Summary

Over our first 20 years, we have undertaken over 70 systematic reviews, created two evidence libraries, and hosted and taught many clinical fellows. Our focus for the next few years is to continue what we have started. Specific projects in the next two years are to continue to build our relationship with ISBT, review our priority areas by updating our James Lind Alliance priority-setting partnership exercise and build our own website to have a central resource to disseminate our activities and improve our engagement with anyone interested in the practice of transfusion medicine.

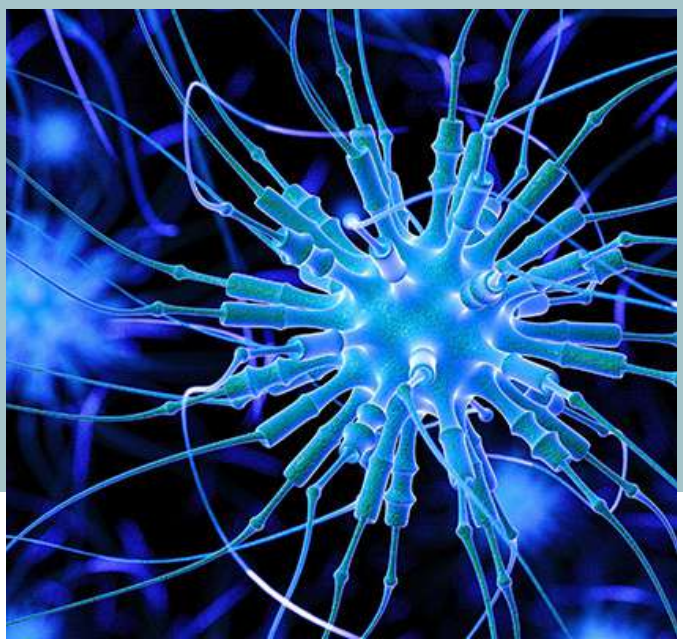
Please follow us on Twitter: @sritransfusion, @evidencestemc, @transfusionlib.

References available on our website.

Susan J Brunskill
Senior Information Scientist and SRI Manager Systematic Review Initiative and NHS Blood and Transplant, Oxford

Lise J Estcourt
Consultant Haematologist, Associate Professor of Haematology and Transfusion Medicine, Clinical Lead for the National Comparative Audit in Blood Transfusion, Director of NHSBT Clinical Trials Unit, Director of Systematic Reviews Initiative and Associate Medical Director University of Oxford and NHS Blood and Transplant, Oxford

RETURN TO CONTENTS



Virologists are doctors and scientists who oversee the diagnosis, management and treatment of patients with viral infections. Virologists are also involved in public health – studying and advising on infections spreading globally as a result of travel and climate change. Some virologists specialise in vaccine development. This specialty has been particularly recognised in making an enormous contribution to COVID-19 testing and diagnosis, as exemplified here by Dr Noha El Sakka OBE.

Dr Noha El Sakka OBE

The Scottish Diagnostic Virology Group: reflections from the current Chair

The Scottish Diagnostic Virology Group has been active for more than 60 years. During the College's Diamond Jubilee year, the current Chair reflects on the history of the group and how scientific virology has evolved and thrived, now achieving even greater levels of success.

Who are we?

The Scottish Diagnostic Virology Group (SDVG) is the only specialist clinical virology scientific group in Scotland. Membership spans the full spectrum of the diagnostic virology community, including medical consultants, clinical scientists, biomedical scientists and trainees.

History of the group

The SDVG has an interesting history. I took over the role as Chair of the group in 2016 and, while I was always aware of its long and rich history, I knew little beyond this. That is until December 2017, when a yellow envelope arrived in my pigeon-hole as a very kind New Year's present. This was from one of the early founders of the SDVG who used to be the secretary of the group in the 1970s. The envelope contained an amazing historical collection of the SDVG (work, archives, memoirs) dating back to 1960, when the group originally formed.

So, it all started in 1960 (62 years ago) with Professor M Stoker's idea to generate a Clinical Virology Group in Scotland. The group's purpose was to interchange information on techniques, methodology and potential collaborative research. Members of the group (around 40 members) were clinical virologists from Aberdeen, Dundee, Edinburgh, Glasgow, Inverness and Newcastle.

The name was later changed to its current one in 1964. The group met regularly twice a year (May and November) in a tradition that remained until it was temporarily paused in 2020 due to the COVID-19 pandemic.

Going through the historic agenda items, minutes and correspondences takes you on an amazing journey through time that reflects the scientific developments that have occurred in the field of virology, and makes you appreciate the level of knowledge we have reached in modern times.

Topics of discussion included: the difficulty resourcing enterovirus antisera for diagnostic purposes and reaching out to the World Health Organization when they were still unable to supply it, finding a suitable cell line for viral cultures, sterilisation of calf serum for use in tissue culture medium, electron microscopy for virus detection, and the introduction of fluorescent antibody assay for virus identification in routine diagnostic labs. Outbreaks of poliomyelitis, measles and rubella infection were also included among many other

RETURN TO CONTENTS

discussions. It is also interesting to see lots of research around zoonosis and virus infection in cattle and sheep by the Morden Institute.

There was some excitement around the morphology of coronavirus in the 1970s. Little was known at that time about how this would progress in the future.

> One can only respect and appreciate the outstanding effort and dedication of the diagnostic virology community since the 1960s...

Reflection on the advances in science and technology

Looking back through the timeline, it is very satisfying to observe the gradual progression of scientific and technological developments. Many of the young virology generation nowadays will not have experienced the original methods used in a diagnostic lab. A quick comparison to a modern-day SDVG meeting agenda puts the change into perspective: molecular assays, genotyping, antiviral resistance assays, point of care PCR and next generation sequencing – in addition to laboratory accreditation and the practice of audits, quality improvement projects and compliance with modern laboratory quality standards.

Additionally, some viruses have now been eradicated (e.g. smallpox) and are not part of the testing repertoire anymore. On the other hand, there are viruses that were not known to us in the 1960s (e.g. HIV, HBV, HCV) and are now part of the standard testing and screening repertoire of virology diagnostic labs.

Reflection on the efforts made

One can only respect and appreciate the outstanding effort and dedication of the diagnostic virology community since the 1960s, pulling the strings together and creating an efficient and professional network. The likes of Professor Dick Madeley, Dr Moffat, Dr Ross, Professor Grist and many others all persevered to maintain close links between the different Scottish labs in order to collaborate with others and communicate with external bodies using one voice.

We owe a lot of where we are now to the effort and dedication of this early team. It is great to see how this culture of professionalism and dedication has continued and become established practice among the SDVG. This type of network has contributed significantly towards keeping the scientific community in Scotland up to date, allowing young scientists to thrive, making way for areas of collaboration and providing a good platform for the exchange of knowledge and expertise.

SDVG today

The SDVG has maintained its original structure while naturally evolving to expand its membership and scope. The SDVG symposium is now recognised and accredited by the College and the Institute of Biomedical Science as an approved CPD activity. Members of the group have made significant efforts to bring in research opportunities, and build more connections and networking across diagnostic labs in Scotland.

The SDVG symposium, a free event organised twice yearly, is popular and attracts all categories of staff involved in the clinical virology service. We also attract colleagues from health protection, epidemiology, veterinary and academic research groups. Beyond Scotland, we invite speakers and delegates from across the UK to contribute and exchange their research and experience with the SDVG community.

Members are invited to present interesting or unusual clinical cases, technical problems, audits and new developments, not only limited to viruses, as many virology labs test for a range of pathogens. Similarly, epidemiology, lab organisation, infection and quality control are all of significant interest to the audience. The symposium is a great opportunity for trainees to promote their work to a friendly, informed audience. A taste of modern topics include hepatitis C treatment and resistance testing, sequencing for HIV outbreak investigating and influenza point-of-care testing for winter pressures.

One of the key strengths of the SDVG symposium is the commercial trade exhibition organised annually, thanks to my predecessors. The exhibition provides an excellent platform where trade companies showcase state-of-the-art kits and instruments in the field. The symposium provides a great opportunity to meet diagnostic virologists and microbiologists from Scotland. The exhibition has contributed to introducing lots of new technologies, studies and research in the virology diagnostic labs in Scotland.

It is a pleasure to present the success of the SDVG over more than 60 years. It has been a valuable lesson to learn how working and collaborating in a network is the way forward to enrich knowledge, science and clinical services.

Read our latest updates on Twitter: @SDVG_

Dr Noha El Sakka OBE
Consultant Medical Microbiology and Virology
Chair of the Scottish Diagnostic Virology Group
NHS Grampian, Aberdeen

RETURN TO CONTENTS

Plants and pathology during the College's Diamond Jubilee celebrations

Dr Shubha Allard

As a keen gardener and an even keener haematologist, *Bulletin* Editor Dr Shubha Allard combined her interests to organise events around the theme of 'Plants and pathology' during the College's Diamond Jubilee year, involving the Royal College of Physicians and the Royal Horticultural Society.

Royal College of Physicians' medicinal garden tours

The Royal College of Physicians' (RCP) garden of medicinal plants contains an impressive 1,100 plants, all with a medicinal connection going back through the ages. Many of these are referred to in England's first pharmacopoeia, the Pharmacopoea Londinensis, published in 1618. Many have been used as herbal medicines around the world with around 50 or so used to make modern medicines.

The garden has a wonderful location opposite Regent's Park in London and is arranged according to the continent of origin, from North America, Europe, the Middle East and countries of the southern hemisphere together with an arid zone and a Classical bed.

College members from a medical and scientific background joined small group tours of the medicinal gardens with highly expert and engaging commentary from knowledgeable RCP garden fellows such as Dr Henry Oakeley (who wrote an article on medicinal gardens in the April 2022 *Bulletin*) and Dr Noel Snell.

We learnt a lot about exotic plants as sources of toxins or medicines, such as vinca alkaloids isolated from the leaves of the Madagascar periwinkle plant, *Catharanthus roseus*, formerly known as *Vinca rosea*, to common garden varieties such as Euphorbia (spurge) which is highly irritant. Several entertaining anecdotes rapidly filled the 1.5-hour tour and we all left with some lively tales and a new respect for plants either as friend or foe.

Discussing plants and allergy at the Royal Horticultural Society Wisley Hilltop science centre

The Royal Horticultural Society's (RHS) Hilltop centre at RHS Wisley is referred to as 'the home of gardening science' and is the UK's first dedicated horticultural scientific centre of excellence open to the public. It strives to inspire the next generation of scientists with the key aims of protecting the future of plants, people and the planet.

Encompassing the RHS Hilltop centre are various new gardens (Wellbeing, World and

Flowering Madagascar periwinkle plants at the RCP medicinal garden.

RETURN TO CONTENTS

(Above) Dr Yong and Dr Kumararatne presenting on plant allergies, visited by *Bulletin* Editor, Dr Shubha Allard.

(Right) Garden fellow, Dr Henry Oakeley.

Wildlife), reflecting the latest research for people to take away and incorporate at home and in schools. There are also showcase displays and interactive exhibits featuring world-class collections. The RHS Herbarium holds the UK's largest collection of cultivated plants, with more than 86,000 dried plant specimens.

It was a pleasure to organise a talk on behalf of the College with Dr Patrick Yong and Dr Dinakantha Kumararatne, both highly experienced consultant immunologists, speaking on the topic of 'Plants and allergy' as part of the 'Hilltop Live' programme. The audience consisted of visitors to the garden and RHS staff who were all captivated by highly informative and expert talks.

Dr Yong spoke on the alarming increase in rates of allergy to plants and food, especially in the western world, together with possible causes. Dr Kumararatne then spoke about mechanisms of reactions on contact with plants and their context in gardens, open spaces and occupational settings. The talks were accompanied by a lively interactive quiz with many challenging questions arising as part of the discussion.

We will aim to organise further talks given by College members at the RHS Hilltop centre next year. Please contact me if you have ideas for talks and are interested in participating.

Dr Shubha Allard
***Bulletin* Editor**

RETURN TO CONTENTS

An antimicrobial stewardship education collaboration between the National Postgraduate Medical College of Nigeria and the Royal College of Pathologists

Dr Kenneth Iregbu

Kelley Price

Professor Angharad Davies

As part of a Memorandum of Understanding between the National Postgraduate Medical College of Nigeria and the College, a series of interactive online events delivered antimicrobial stewardship training to Nigerian healthcare professionals. In this article, we hear more about antimicrobial resistance in Nigeria and about the lecture series.

The global effect of antimicrobial resistance

Antimicrobial resistance (AMR) is a global issue. A systematic analysis of the global burden of AMR published earlier this year reported 4.95 million associated deaths and 1.2 million attributable deaths from bacterial AMR infections in 2019.[1] Today, AMR endangers the efficacy of life-saving antimicrobials, moving us towards a post-antibiotic era, where treatment of multidrug-resistant infections may become impossible. This trend can only be halted through global actions and concerted efforts, including implementation of antimicrobial stewardship (AMS) at care facilities.

AMR in Nigeria

Nigeria has documented the occurrence of AMR in microbial populations across humans, animals and the environment. However, reports of AMR infections in Nigeria are often inaccurate, making it difficult to provide comparable AMR data on a continuous basis. Reasons for the inaccuracy include poor surveillance systems to document patterns and trends of infectious diseases, and inadequate microbiology laboratory capacity in terms of standardised protocols and external quality assurance. The drivers of AMR in Nigeria are well known. They include misuse of antimicrobials caused by inappropriate prescribing practice among healthcare practitioners, overuse of antimicrobials in agriculture, aquaculture and veterinary sectors, and failure to enforce regulations on antimicrobials procurement and distribution. For example, antimicrobials are available over the counter to the populace.

To combat the challenge of AMR, in 2017, a situational analysis of antimicrobial use and resistance in Nigeria in the agriculture, environment and health sectors was conducted.[2] This was coordinated by the Nigeria Center for Disease Control (NCDC). This was then followed by strengths, weaknesses, opportunities and threats (SWOT) analyses, which provided a clear strategy for the development of a five-component 'One Health' national action plan (NAP; 2018–2022) for the country.[3]

Coordinated implementation of the AMR NAP[4] in Nigeria has been severely hampered by poor funding, poor infrastructures (especially at primary and secondary care facilities), poor coordination and a lack of serious governmental commitment. Implementation has therefore been restricted, largely being driven by the Clinical Microbiology and Infectious Diseases Society of Nigeria (CLIMIDSON).

Collaborative training

To help further the implementation of the AMR NAP, the Faculty of Pathology at the National Postgraduate Medical College of Nigeria (NPMCN) and CLIMIDSON worked alongside the Royal College of Pathologists to deliver a series of events covering AMR and AMS. The aims of the series were to provide participants with information on the current situation of AMR globally and across Nigeria and the UK; provide information on establishing an AMS program, developing policies and guidelines, implementing strategies, monitoring and evaluating, and sustainability in developing and developed climes; and highlight the challenges of AMS implementation in a low-resource setting such as Nigeria.

Dr Kenneth Iregbu
President, CLIMIDSON & Chief Consultant Clinical Microbiologist, National Hospital Abuja, Nigeria

RETURN TO CONTENTS

Design of the online event series

From the outset, the training was designed to be interprofessional. NPMCN invited healthcare professional teams from healthcare settings across Nigeria to attend, including medical microbiologists, nurses, pharmacists and physicians working in infection. The event series ran for six weeks, and expert speakers from both Nigeria and the UK spoke at each event. The format of each session consisted of a 20–25-minute presentation on a topic by a Nigeria-based expert, followed by a presentation of a similar length by a UK-based speaker, allowing different contexts, approaches and settings to be considered, compared and discussed. Nigerian expert speakers were identified by NPMCN, and UK speakers were identified by the Welsh Antimicrobial Pharmacy Group, also drawing on UK Health Security Agency (UKHSA) expertise. After a short break, a Q&A session followed in which the audience could ask questions and share their experiences.

The need to embrace AMS as a key intervention in combating the challenges of AMR was a key message throughout the events. A range of topics were covered including the implementation of AMR and AMS programmes in primary and secondary care settings, the development, implementation and monitoring of antimicrobial policies and guidelines, engaging of the public in AMR and AMS and changing behaviour, making AMR and AMS education in clinical settings sustainable, and identifying key challenges and barriers to AMS implementation.

Evaluation and future plans

The event series received excellent feedback from delegates. Around 100 delegates attended each event and all evaluation respondents said that, as a result of the event series, they would introduce or consider introducing new measures for better AMS.

The format of the sessions was particularly valued, with 100% of respondents agreeing that this was successful and beneficial.

"Having speakers from the UK and Nigeria was a great idea because participants were able to have access to the experiences of the speakers from different countries, thereby giving them a broader perspective to AMS."

"It gave a sense of belonging and ownership to have Nigerian-based speakers."

"All participants were carried along and we got to know the perspectives from both sides."

"Alternating the presenters made a valuable mix, allowing for the interface of experiences from different backgrounds."

It is planned to build on the success of this series by running a second series in 2023. Delegates have indicated they would like to see the following topics included in future series: applying laboratory stewardship in clinical practice, AMS and surgical prophylaxis, surveillance and data analysis, and formulating and implementing policy on AMS at a national level.

The College is very grateful to the expert speakers from the UK and Nigeria who volunteered and generously gave their time for this project.

References available on our website.

Kelley Price
RCPath International Projects Officer

Professor Angharad Davies
Vice President for Learning & International

International Pathology Day 2022

Our 2022 International Pathology Day (IPD) will celebrate the College's Diamond Jubilee and explore the theme 'Adapting laboratory medicine to global developments and challenges'.

Together with our event sponsors – the British Society for Haematology and *The Pathologist* – we invite you to join us, either in person or virtually, on Tuesday 1 November for a hybrid conference. This is in advance of the official day of celebration for IPD. The conference will take place in the College's building at 6 Alie Street, London, and registration for in-person attendance will be at 9.15am. The conference will run until 2.30pm.

The programme includes a range of talks from four speakers, including special guest and keynote speaker Dr Michael Ryan, Executive Director, WHO Health Emergencies Programme, who will join us virtually. Our signature roundtable discussion will explore the international activities of the College in a changing world – past, present and future. There will also be a poster competition open to both international and national entrants.

For more information and to register your place to attend in person or virtually, please visit our website here.

RETURN TO CONTENTS

Neurodiversity and specific learning difficulties in training and the workplace: why do they matter?

Dr Liz Hook

Dr Rachel Rummery

This article reflects upon neurodiversity and specific learning difficulties from the perspectives of the pathology trainer and trainee. Dr Liz Hook emphasises the need for the College and pathology trainers to recognise these conditions, while Dr Rachel Rummery offers a personal account of her experiences.

Neurodiversity is the term used to describe the wide differences in the interactions and experiences that individuals have with others and the world in general.[1] The term encompasses specific conditions including autism spectrum disorder and attention deficit hyperactivity disorder (ADHD). Specific learning difficulties (SpLD), including dyslexia, dysgraphia, dyscalculia and developmental coordination disorder (dyspraxia), describe differences in the ways in which an individual interacts with and processes information that affect different aspects of learning.[2]

In 2018, the General Medical Council published *Welcomed and Valued*,[3] a document laying down an advisory framework for supporting individuals with disabilities including SpLD and neurodiversity in medical education and training. As this document highlights, there is a requirement to comply with UK equality legislation and also with GMC standards for medical education and training.

The pathology trainer's perspective

Dr Liz Hook is a university lecturer in cellular and molecular pathology and an honorary consultant paediatric pathologist at Cambridge University Hospitals NHS Foundation Trust. She is the senior examiner for clinical pathology at the University of Cambridge and, having received additional training in facilitating learning for students with ADHD and SpLD, works closely with medical students with ADHD and/or SpLD to support their studies.

Why is this important for trainers and programme directors?

In higher education, the number of students with a diagnosis of SpLD and/or neurodiversity is increasing.[4,5] Best practice now entails promoting early diagnosis of these conditions. Institutions are encouraging students to undergo educational/learning assessment if potential issues are identified.

Diagnosis of an SpLD and/or neurodiversity is then followed by the adoption of reasonable adjustments in learning and examination environments to afford equity by removing barriers that disadvantage the individual owing to their condition. Examples of reasonable adjustments include additional time for assignments, 1:1 coaching from a trained professional, early access to teaching material and variations in examination conditions.

Doctors in training who find the FRCPath examinations challenging may have existing or undiagnosed SpLD and/or neurodiversity, which can be subsequently identified on assessment. Early assessment and support are best encouraged by increasing awareness among trainers and doctors in training, by local signposting and with easy access to assessment, usually via local Health Education England (HEE) Deanery Professional Support Units. However, diagnosis alone is not sufficient and appropriate support needs to be offered after this, including targeted educational input to identify areas that the individual finds especially challenging.

In my opinion, in addition to standard neurodiversity/SpLD coaching, input from a subject matter specialist who has received training in supporting learning for individuals with neurodiversity and/or SpLD may be beneficial. In particular, such trainers can provide specific insight concerning approaches to assessments.

Why is neurodiversity important to the College?

Key considerations for the College about training and assessment for individuals with SpLD or neurodiversity focus on curriculum and assessment design, including the consideration of reasonable adjustments, a role highlighted in *Welcomed and Valued*.[3] Ideally, however, widespread adoption of universal design for learning would ensure that teaching, training and assessment are accessible to as many as possible. The principles of universal design for learning focus on creating inclusive teaching and environments that remove as many barriers to learning as possible.[6]

The College's involvement in both training and workforce means this is a highly pertinent issue. The

RETURN TO CONTENTS

provision of pathology discipline-specific advice for trainees, trainers, programme directors and ultimately clinical directors could move the College to the forefront of ensuring equity across the workforce for individuals with SpLD and neurodiversity.

The current model for consultant appointments requires individuals to negotiate any reasonable adjustments required with their clinical leads and occupational health departments. An advisory guide provided by the College suggesting recommendations for workplace accommodations could suggest a supportive blueprint of reasonable adjustments and an evidence base for individuals to negotiate with their local employers.

The starting point for this process should be supporting members who have an SpLD and/or neurodiversity to talk with the College about their experiences in the workplace and highlight both helpful adjustments and also aspects of the workplace that remain challenging.

Why is this important for the consultant workforce?

Increasing recognition of SpLD and/or neurodiversity in medical student cohorts[4,5] will be mirrored across the medical workforce over time. Provision of supportive and appropriately adjusted working environments may lead to reduced consultant burn-out and improved job satisfaction and, thus, retention of individuals within the consultant workforce.

Suggestions for development

The College has already made a number of positive changes with the commissioning of a strong Equality, Diversity and Inclusion Network by the Trustee Board and the hosting of informative events such as the recent webinar panel discussion *Improving disability adjustments in pathology: current perspectives and looking to the future*. However, there is more to be done and I would make the following suggestions to encourage open discussion on this important topic.

Regarding training, information about SpLD and neurodiversity and how to seek support and assessment should be provided on the College training pages. Ensuring identification and dissemination of excellent practice across different training programmes could be achieved via the Trainees Advisory Committee. Universal design for learning principles should be applied to curricula, assessment and workplace standards.[6]

In *Welcome and Valued*,[3] it is suggested that reasonable adjustments should be reviewed to ensure that the desired results are achieved; if an adjustment is declined, the suggestion is made for an audit trail to be kept to give evidence of decision making. For high-stakes situations around assessment, this might be best achieved with a multidisciplinary review committee.

Finally, visibly demonstrating that everyone is welcomed and valued within the UK pathology community will benefit our workforce as a whole.

The contents of this article have been shared with the College Learning directorate, which will consider the various suggestions raised.

The trainee's perspective

Dr Rachel Rummery is an ST6 trainee in paediatric and perinatal pathology at Yorkshire and the Humber Deanery. She is also the current Vice-Chair of the College Trainee Advisory Committee.

Personal experience of neurodiversity as a trainee pathologist

After Liz's experienced insights into the overarching organisational importance of neurodiversity and SpLD, it falls to me to give my personal view of their effects. I have no expertise in this area and my thoughts can only reflect my own experiences.

I have had an eclectic career. I did my undergraduate medical training at the University of St Andrews, then Trinity College, Cambridge. I was a pathology lecturer and honorary registrar in the 1990s, then took a career break to look after my children before returning to medicine in 2011. I re-entered the histopathology training programme in 2013 and moved to paediatric and perinatal pathology after my FRCPath Part 1.

Wanting to use my experience of returning to medicine (which wasn't easy) to help others, I became one of the inaugural Health Education England (HEE) Supported Return to Training fellows in 2018. Then, alongside training, I became the HEE Clinical Lead for Return to Practice (see Dr Rummery's article on this in the April 2020 *Bulletin*). In this role, during the pandemic, I worked with NHSE/I on the Bringing Back Staff initiative. I also instigated the launch of the HEE CaReForMe return programme[7] and worked with the General Medical Council to produce the *Completing the Picture* survey, the world's largest study of why doctors leave medicine.[8,9]

The difficulties that neurodiverse trainees can face

The relevance of this career path is to highlight how hidden neurodiversity can be. Until my ST5 training year, there was no reason for either me or my trainers to consider that I might have any SpLD or neurodiversity. I had never failed an exam or had less than an ARCP outcome 1. However, as my FRCPath Part 2 exam approached, I realised, as I looked at the various elements, that I was going to find the format very difficult – or if I was honest with myself – impossible.

Initially, I was concerned I would not be able to write fast enough, so perhaps I had an element of dysgraphia. I took a deanery-approved screening test, which instead highlighted working memory, processing speed and attention issues. I then had a formal educational psychologist assessment which

RETURN TO CONTENTS

diagnosed dyspraxia (developmental coordination disorder) and probable inattentive attention deficit disorder (ADD).

In many ways, my diagnosis has been nothing but positive. I realised, as I looked back through my life, that it explained so many things: the annual school reports that were all variations on a theme of 'able but slow and a bit lazy'; my inability to take minutes or lecture notes (I bought the textbooks); and why I found writing long reports (including scientific papers) very hard, especially in one sitting – I tended to break work down into manageable chunks.

On a personal level, it explained apparently trivial things like why I take a long time to cross the road (I process the speed of traffic slowly), and why I can't follow board game rules (my working memory is too poor) or play fast-paced computer games (my processing speed is too slow). Physically, I've never been able to play team sports, kick or catch a ball and I still have an odd way of tying my shoelaces. The realisation that my various difficulties are not laziness has finally allowed me to be kind to myself.

The impact of support

So, I didn't doubt the diagnosis was correct, but it was still a shock. I'd barely ever heard of dyspraxia or ADD/ADHD. I've always been a very independent person, so I found reaching out for help hard. But I did ask for help and I got it – in spades! I have had truly stellar support from my educational supervisor, mentor, trainers, deanery, sub-specialty exam panel and colleagues in the College. I am on the Equality, Diversity and Inclusion Network and was a panellist in the webinar that Liz mentioned above.

My deanery has provided neurodiversity coaching and time for mentoring, all of which have been very useful, providing insights that are useful not just for training but for future working, making me more efficient and confident. The adjustments I need in my working day are actually very minor – report templates, a desk that faces the wall, noise cancelling headphones, voice recognition and a chair for post mortems/surgical cut up. But they have made a massive difference.

I am also more aware of my strengths. A lifetime of unconsciously using my perceptual reasoning and verbal comprehension to compensate for my working memory and processing speed means that, like many neurodiverse people, I enjoy out-of-the-box and big-picture thinking, something I have found very useful in my leadership roles.

The hardest thing to come to terms with has been the gradual realisation that, while understanding, support, coaching and self-compassion are all incredibly useful, they cannot 'fix' me. I cannot change my cognitive profile. It is as much part of me as a more physically manifested disability.

This means that, after three attempts, I have so far been unable to pass my Part 2 exam, although I have passed all the elements at some point.

Liz is right that awareness and acceptance are key. I very much wish I had known earlier. Hopefully, sharing my story is a small step along this road and will help others. I wish to thank the College for being so proactive in engaging with this topic, and Liz for so generously giving us the benefits of her expertise.

References available on our website.

Dr Liz Hook
University Lecturer in Cellular and Molecular Pathology, Honorary Consultant Paediatric Pathologist
Cambridge University Hospitals NHS Foundation Trust

Dr Rachel Rummery
ST6 Trainee in Paediatric and Perinatal Pathology
Yorkshire and the Humber Deanery

RETURN TO CONTENTS

Research in pathology: medical students' experiences

Undergraduate medical students often hear about research at their universities but sometimes struggle to get involved. Here, six medical students share their experiences in a wide range of research projects led by pathologists around the country. The students also suggest some tips and advice for researching clinicians.

All these students received funding through the Pathological Society of Great Britain and Ireland. Dr Gemma Petts, Undergraduate Lead for the Pathological Society of Great Britain and Ireland, facilitated the writing of this article. Other funding opportunities are available from the likes of the British Neuropathological Society (BNS) and the INSPIRE programme.

Dr Gemma Petts
Undergraduate Lead
Pathological Society of Great Britain and Ireland

Abraham Tolley

A formative experience in medical research

Abraham Tolley from Cambridge University worked with Dr Anna Protasio's group for six weeks during his summer break.

I spent my time conducting both wet-lab and dry-lab work. I learnt and then carried out experiments in RNA biology to explore the schistosomiasis parasite. I also conducted dry-lab bioinformatics research using Unix/Linux and R to explore vaccinia virus infection of human cells. This was an amazing experience, where I learnt much about the process of scientific research and gained a myriad of skills.

I planned and implemented experiments, including PCRs, gel electrophoresis and extraction, transformations, and mini-preps. I also developed my ability to interpret experimental results to determine appropriate subsequent investigations. Furthermore, I improved my bioinformatics skills by implementing a multi-step processing pipeline that involved interacting with computer cluster systems for large dataset processing and analysis, as well as using available literature to inform experimental decisions.

The opportunity to work with the Protasio group was a really formative personal experience that has led me to subsequently carry out wet and dry-lab research, as well as explore options for further research opportunities in my future medical career.

Grace Farnworth

Gaining insight from practising researchers

Grace Farnworth from Leeds University worked with the National Pathology Imaging Co-operative (NPIC) for seven weeks of their summer break.

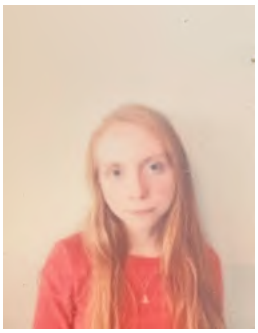
I completed a research project in digital pathology, comparing Breslow thickness measurements of melanoma specimens on both glass slides and digital whole slide images. This work enabled me to get involved in the exciting area of digital pathology.

Digital pathology presents many new possibilities, such as remote working, easier data/image sharing and use of artificial intelligence. I experienced first-hand the differences between digital and light microscopy, including their own unique benefits and drawbacks.

During my project, I was able to ask different professionals about their preferences between the two, which was very insightful. Observing some of the histopathologists carry out their work enabled me to see the clinical relevance of my project, a chance that otherwise would not have been available to me in my standard curriculum.

The project gave me the opportunity to work independently, building upon key skills such as self-directed learning, knowing when to seek advice from others and problem-solving. These skills are not only useful for carrying out more research, something I hope to do, but will be hugely beneficial to my studies and medical career in the future.

RETURN TO CONTENTS



Jennifer Glass

Enriching knowledge and enthusiasm for pathology

Jennifer Glass from Leeds University worked with Pathology and Data Analytics, Leeds Institute of Medical Research at St. James' Wellcome Trust for five weeks during her 2021 summer break.

I undertook a project investigating the localisation of Grb-2 and PLC-γ in lymph nodes from cancer tissue using immunohistochemistry, in combination with immunofluorescence, to perform confocal microscopy and direct stochastic optical reconstruction microscopy (dSTORM). It was a privilege to use the dSTORM microscope and gain experience of the scientific and laboratory techniques employed.

During the project, I developed an appreciation for how much preparation is required in the lead up to imaging samples. I came to understand the complexity of capturing images at such high magnification in terms of orientation and staining quality. As a medical student, it is easy to take for granted the images we see in textbooks and lectures. Carrying out this project has given me a greater understanding of the different types of imaging and how they can provide us with the means to expand the boundaries of pathology research.

The experience has not only enriched my medical knowledge, but also sparked an enthusiasm for pathology research and learning more about the applications of dSTORM microscopy in research and clinical practice.

Top tips and advice

Here are some top tips and advice for those wanting to involve medical students in research projects:

1. Advertising: If you are seeking students for involvement in research projects, advertise these opportunities at the beginning and/or end of lectures, seminars and tutorials. Most medical schools have some kind of weekly newsletter or online promotional area/noticeboard for medical students. It is also possible to advertise projects through student societies or places like the INSPIRE programme, which may reach medical students from outside your own institution.
2. Timeframe: Long summer breaks tend to be a better time for medical students to get involved in research projects. You may need to consider that most, if not all, the work will need to be carried out within the summer months or another specific time.
3. Variety: Laboratory-based project work is only one form of research that medical students may be interested in – consider offering opportunities to join in reviews, data analysis projects, audits or quality improvement style projects as well.

Peter Robinson

Developing academic skills

Peter Robinson from Newcastle University worked with the Cellular-Molecular Pathology Group at the National Cancer Research Institute for eight weeks during his summer break.

The project involved assessing the inclusion of SPIRIT-Path guidelines in clinical trials supported by the Cellular Pathology department at Newcastle upon Tyne Hospitals. SPIRIT-Path describes the minimum pathology content for trial protocols and is an extension of the original *Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 Statement.*

Taking part in this project has been rewarding and has made me aware of the challenges in research, such as responding and reacting to new information. Having numerous opportunities to receive feedback from experts has highlighted the importance of collaboration in maximising the information gained from a study. Speaking with laboratory staff and pathologists allowed me to gain an insight into their role in the smooth running of trials, such as the preparation of specimens and molecular analysis for determining patient inclusion criteria and assessment of trial outcomes.

The project gave me the opportunity to develop my academic writing skills through preparing a draft manuscript outlining the methodology and results and discussing the significance of the findings. I was also lucky enough to experience one of the rewards of research, with the paper being published in the *Journal of Pathology: Clinical Research*.

RETURN TO CONTENTS

Alexander Matthews

Presenting research at a conference

Alexander Matthews from the University of Bristol spent six weeks in the Department of Neuropathology at Southmead Hospital carrying out a summer project.

I carried out a project on whether certain primary brain tumours could be distinguished using an immunohistochemical stain for the presence of the epigenetic marker H3K27me3. The results of the project were accepted for oral presentation at the 123rd Annual Conference of the British Neuropathological Society.

I remember feeling a delicate balance of excitement mixed with terror when I received this news. I had never done anything like this before. My first port of call was to discuss what should be included in the talk with my supervisor. She was highly supportive and advised me simply that my audience, pathologists, like facts and figures, so I should include good summaries of the data in graphs and images. I followed this advice and, three drafts later, the slides were ready.

I have received numerous talks regarding the common experience of impostor syndrome while at medical school. This was the first time I felt this so strongly and I was nervous about the presentation right up until the day of the talk.

The presentation itself went well enough. It was delivered via an online platform to hundreds of subject experts, including my supervisor and head of department. I was pleased to be able to answer all questions bar one in the subsequent Q&A session for my talk. My supervisor and head of department both gave me positive and complimentary feedback, which felt great.

I've always been sceptical about the saying that you know your own work best, but maybe there is some truth to it after all, even as a medical student. Overall, it was an excellent experience and one I would highly recommend to others should they find an opportunity.

Top tips and advice

Here are some top tips and advice for those wanting to involve medical students in research projects:

1. Foster independent working: Given a relative lack of experience, medical students will likely need support in working on projects you have designed or suggested. However, it is beneficial to create a supportive environment where the student can take ownership of the project. This gives them the opportunity to develop communication skills, critical thinking, teamworking, empathy, problem solving and creativity, alongside the technical skills of the project.
2. Publication and presentation: Medical students may value opportunities to be involved in publications and presentations. These are both important learning opportunities for them and potentially valuable portfolio material. Projects with these opportunities may be particularly attractive to medical students.

Jonathan Callaghan

Learning from interdisciplinary experts

Jonathan Callaghan from Queen's University Belfast spent eight weeks with Cirdan during his final year summer elective.

I spent most of my final year summer elective placement with Cirdan, a global pathology imaging and informatics company based in Northern Ireland. I sought out this industry experience to complement my previous histopathology experience and deepen my understanding of the academia–industry intersection.

I was based with the artificial intelligence (AI) research team and gained exposure to various parts of the pathology solutions company. It was eye-opening to work with colleagues who had backgrounds in engineering or computer science. Interestingly, many had experience of using AI tools in industries unrelated to pathology or healthcare. We therefore learnt much from each other.

I assisted with their understanding of annotated slides, certain diseases or clinical and laboratory pathways. I also learnt some basic Python coding skills and gained some understanding of the challenges faced in the algorithm development, such as testing and validation.

My experiences underlined to me the importance of interdisciplinary working in translational research. This opportunity also gave me a better appreciation for the existing limitations and capabilities of AI tools, in particular how they hold tremendous value and potential but should not be perceived as a panacea.

My time at Cirdan also gave me insight into the world of business, which I found interesting to contrast with clinical and academic environments. I enjoyed learning about product development and delivery, meeting customers' needs, quality assurance and the importance of regulations in this area. This experience has undoubtedly cemented my desire to work in the exciting field that is histopathology.

RETURN TO CONTENTS

Ethics, digital pathology and AI: the importance of the patient and public voice

As the use of and reliance on AI becomes increasingly embedded in working practices, including digital pathology, there needs to be ongoing and meaningful engagement with patients and the public. Here, the College's Lay Advisory Group discusses the ethical implications of AI.

As the UK government seeks to position the UK as a global leader in artificial intelligence (AI),[1] a recent paper has highlighted the ethical challenges of AI-driven digital pathology.[2] This paper is a timely reminder that these ethical challenges are far from resolved. Maintaining the patients' and public's trust is critical; without it, there is a risk that the benefits of AI digital pathology will not be fully realised.

What is AI?

There is no standard definition of AI. The Alan Turing Institute – the national institution for AI – notes that the term AI is often used to 'describe when a machine or system performs tasks that would ordinarily require human brainpower to accomplish... There is a wide range of such systems, but broadly speaking they consist of computers running algorithms, often drawing on data.'[3]

Ethical issues

It is essential to consider the ethical issues when deploying AI infrastructures in pathology. This article focuses on four key ethical issues: privacy, choice, equity and trust. These topics are not intended to be exhaustive and may encompass concepts such as fairness, transparency and accountability. There are, however, a variety of other frameworks that could apply.

Acting in the public interest

Consideration of privacy, choice, equity and trust may be viewed primarily as a way to protect the interests of individuals. But, these are also essential parts of the public interest, which is a key issue that also needs explicit consideration.

There is a public interest in ensuring privacy and trust, for example, so that patients are confident that their interests will be respected when accessing healthcare. This, in turn, ensures good data for research and epidemiological purposes, among other things (whether data is identifiable, pseudonymised or anonymised).

There is also a public interest in research being conducted for the benefit of individuals and society. AI-driven digital pathology has the potential to provide faster, more accurate diagnoses. This would benefit individual patients but also ensure resources are used more effectively, particularly in the context of a depleting UK and global health workforce. When these benefits are highlighted, they are not always couched in terms of an ethical imperative.

Ethical issues from a lay perspective

From a lay perspective, there remain many practical unanswered questions. For example, if I have a rare disorder, can my privacy be guaranteed? What choices will children and individuals who lack capacity have? Will samples, such as genetic material, still need to be retained, raising separate ethical issues? There may be robust information governance in place now, but will this be future-proofed and translated across borders? Are contracts forbidding any attempt to reidentify patients sufficient or do we need additional legislation? Are the data and system secure, for example from cyber-attack?

And lastly, if an opt-out model to use my de-identified data is adopted, can there be conditions? Individuals may be content for data to be used for research purposes to benefit the patient population but may wish to opt out if it is being sold for commercial purposes, particularly if the money received for the data is not ring-fenced to be reinvested in the health service.

Unique considerations

There is a much wider national and global debate on the ethical challenges raised by AI and numerous commitments to address them. The UK Government aims to ensure the UK 'gets the national and international governance of AI technologies right

RETURN TO CONTENTS

to encourage innovation, investment, and protect the public and our fundamental values'.[1]

This debate is distilled down further to individual sectors, for example regarding particular considerations in relation to health. Only last year, the World Health Organization published its guidance, *Ethics and Governance of Artificial Intelligence for Health*.[5] The issue transcends borders.

Further refinement and practical considerations may apply to specific specialties, then specific applications within specialties and systems, to specific purposes – for example medical research.

Many of the top-line ethical considerations will remain the same. While many of the issues are not necessarily unique to AI (such as the challenges of pooling and sharing data for research), it is essential to consider them through the lens of AI so that appropriate mitigation can be built into processes and systems. Additionally, there is a need to think through the issues that occur through the use of AI, such as the need to be able to understand why the results provided by an AI system are what they are (in order to be able to identify inaccuracies/errors made by the system) or the need to understand the datasets used to train the data and get the algorithms to work, in order to address bias/errors in data.

When considering the ethical challenges in AI-driven digital pathology, it may be helpful to look to other specialties that face similar challenges. For example, the Royal College of Radiologists has taken a keen interest in AI. The NHS Lab – which brings together government, health and care providers, academics and technology companies – is now developing a National AI Medical Imaging Platform, following the success of the National COVID-19 Chest Imaging Database that was created to support the NHS pandemic response.

Robust governance and public engagement

There is a need for ongoing patient and public engagement, both for now and in the future, as our understanding of the potential individual and public benefits, risks and harms of digital pathology and AI evolve.

The question is, what does meaningful engagement look like? What role can pathologists take in bringing patients and the public along to ensure the benefits of AI digital pathology are fully realised? And, how can any harm and risks be mitigated?

References available on our website.

Anomika Bedi
Lay Advisor, Royal College of Pathologists

Rebecca Mussell
Lay Advisor, Royal College of Pathologists

Dr Dilek Taze

The histopathological reporting of temporal artery biopsies for giant cell arteritis: results of an RCPath member survey

College member surveys help to clarify uncertainties around current clinical practices. Here, Dr Dilek Taze and Dr Kathryn Griffin explain the outcomes of a recent member survey on the histopathological reporting of temporal artery biopsies for giant cell arteritis.

Background

Giant cell arteritis (GCA) is a serious form of vasculitis that, if untreated, can result in irreversible ischaemic complications, including blindness. Prompt and definitive diagnosis is challenging due to the non-specific and varied clinical presentation and the lack of a robust diagnostic biomarker.[1] The temporal artery biopsy (TAB) is regarded as the gold standard test in GCA diagnosis and forms part of the core diagnostic criteria in all current UK, European and American classification guidelines.[1–3] Furthermore, under current NHS England prescribing guidance, a TAB result is an important component of the eligibility criteria for the novel biologic therapy tociluzumab.[4] Despite the recognised importance of this test, a recently published UK-wide audit of experienced pathologists found a lack of agreement on the diagnostic features and classification of inflammation observed in TAB sections for the diagnosis of GCA.[5] Of the

RETURN TO CONTENTS

Dr Kathryn Griffin

nine micrographs circulated for assessment in this study, only one reached complete agreement in terms of 'bottom-line' histopathological diagnosis.

To further determine the extent of variation and uncertainty in the reporting of TABs for the diagnosis of GCA, our research group Atlas of Histopathology Education for Advancing Diagnostics in Giant Cell Arteritis (AHEADgca) conducted an online survey in June 2021 of all consultant members of the College. The results of this survey are discussed here.

Consultant demographics

We received 116 responses, with 73% of consultants working for an NHS Trust in England and 11% from Wales, Scotland, Northern Ireland or the Republic of Ireland. Ten percent of respondents specified their place of work as 'other', referring to non-NHS practice, and are currently practising diagnostic pathology in Australia, India, Singapore or Pakistan. The remaining 6% did not provide this information.

Of the 116 respondents, 60% had more than 15 years of consultant diagnostic pathology clinical practice. The least common duration of consultant experience was the 0–5 years category with 12% of respondents selecting this option. The remaining 28% fell within the 5–10 or 10–15 years categories.

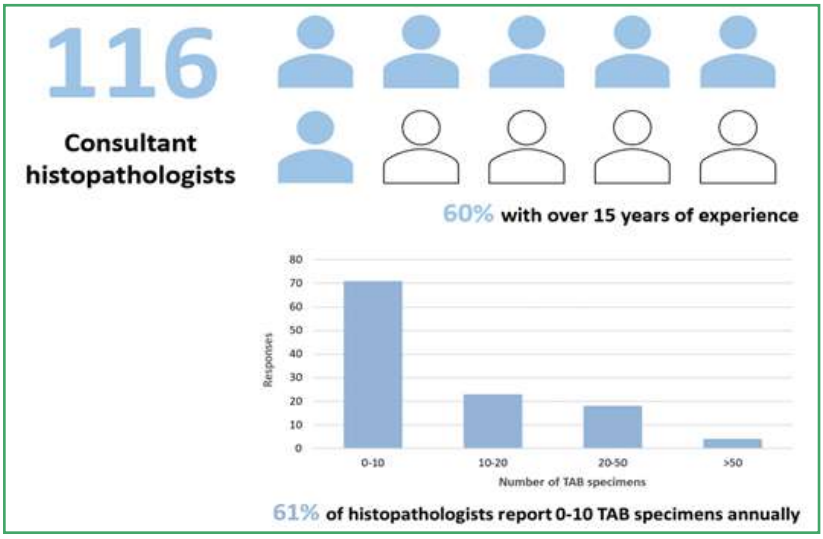


Figure 1. Summary of the RCPath survey consultant demographics and the number of TAB specimens reported annually. TAB: Temporal artery biopsy.

Numbers of temporal artery biopsies reported

Over half (71/116, 61%) of respondents stated that they report fewer than ten TAB specimens per year (see Figure 1). The second most frequent category (20% of respondents) was 10–20 TAB specimens reported annually. Only four individuals specified reporting more than 50 TABs annually, and three out of four of these respondents were neuropathologists working in an NHS Trust in England. Respondents were also asked to provide an estimate for the number of TAB specimens reported annually in their centre, of which the most frequent answer was 21–50 specimens. Interestingly, 20% of respondents were unable to provide an estimate to answer this question.

Clinical information and referral pathways

We asked the respondents to specify how helpful and/or sufficient they find the clinical information provided on the TAB request form. Our results reveal a dichotomy between those who felt that (1) 'We receive enough clinical information, and it is helpful' (49%), and those who answered (2) 'We receive insufficient information and/or it is unhelpful' (51%). We were also interested to determine the number of centres that have a TAB multidisciplinary team (MDT) meeting; 78% of respondents specified that their centre did not, and 19% were unsure. Only two individuals acknowledged a TAB MDT within their centre and further specified this to be a standalone MDT. Of the majority of respondents who answered 'No' to this question, 68% also answered 'No' to there being an established referral pathway for TAB cases requiring a second opinion.

Histopathological reporting criteria for TAB specimens

A key question asked was 'Is the histopathological reporting criteria for TAB specimens clearly defined?'. Nine individuals (8% of respondents) answered 'Yes – there are no issues with the reporting criteria'. Most respondents (98/116, 84%) expressed some form of concern with the reporting criteria or did not provide an opinion. The range of responses is illustrated in Figure 2. Respondents were asked to elaborate on their answers in a free text box and three clear themes emerged from the comments provided.

'There are no reporting guidelines or agreed reporting categories'

While some individuals acknowledged the existence of the RCPath cardiovascular tissue pathways as a useful resource for the handling of TAB specimens, uncertainty was expressed regarding the guidance provided with respect to the histopathological reporting of these specimens for GCA. Other respondents stated that this information is difficult to find or that they were unaware of any published protocols. A suggestion was made for the development of a GCA-specific histopathological reporting pathway with accompanying validated images to improve consistency.

The final question asked in our survey was 'Would an RCPath TAB tissue pathway help you in your practice (similar to those available for other non-cancer specimens)?', of which over half of respondents (75/116, 65%) answered 'Yes'.

RETURN TO CONTENTS

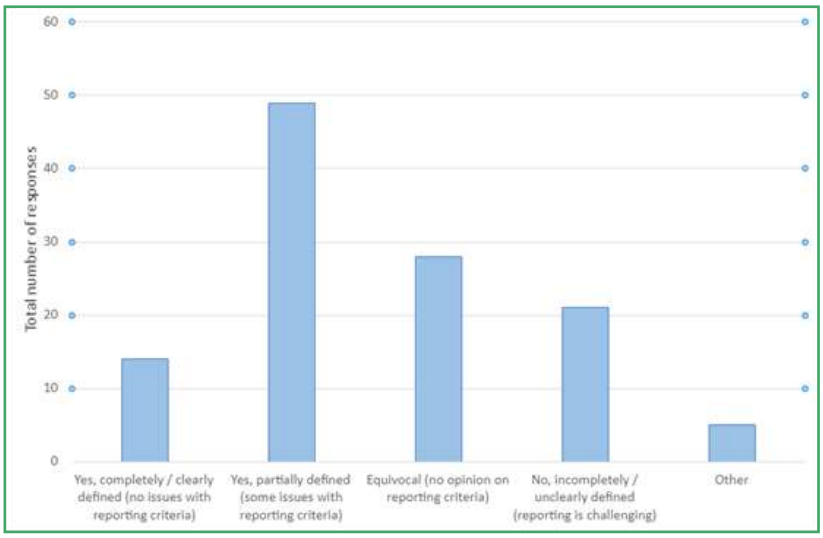


Figure 2. Reponses to the question 'Is the histopathological reporting criteria for temporal artery biopsy specimens clearly defined?'

'There are areas of TAB reporting with no established criteria'

Multiple respondents commented that the criteria for what constitutes 'positive for' or 'consistent with' GCA is not clear, and that there is variation in the interpretation of certain microscopic appearances (i.e. periarteriolar lymphocytic infiltration). Other individuals expressed that the terms 'healed or healing arteritis' are not clearly defined, and guidance needs to be established for when such terms should be used in pathology reports. Another area provoking diagnostic challenge – which was highlighted in our survey – is the difficulty in distinguishing between quiescent arteritis and age-related or degenerative vascular change.

'Timed changes in histopathology due to steroid treatment are undefined'

Some of the respondents made comments regarding the influence of steroid therapy on histopathological appearances at TAB. These individuals highlighted that they are uncertain as to how quickly steroid therapy initiates changes in the biopsy findings and for how long these changes persist. Others made general comments regarding the lack of information provided by clinicians as to when steroid therapy was started and the relationship of treatment to biopsy timing.

Conclusion

Our survey results from the RCPath consultant body have demonstrated that there is variation and uncertainty in the reporting of TABs for the diagnosis of GCA, and there is an expressed need for established reporting criteria. As part of the AHEADgca research group, we have undertaken a modified Delphi study to resolve areas of disconcordance in pathology practice for GCA, and we have demonstrated the potential benefits and acceptability of a standardised reporting protocol. Our research has been submitted for publication and we hope to share our findings with you soon.

Acknowledgements

We would like to thank all our respondents for their time and insightful comments. Your participation is very much appreciated and will help facilitate diagnosis and improve care for patients with GCA. We would like to formally acknowledge all members of the AHEADgca research group for their contributions: Dr Aruna Chakrabarty, Dr Sarah Mackie, Professor Ann Morgan, Ms Collette Hartley and Dr Charlotte Harden. We would like to extend special thanks to Dr Ranjana Venkatswaran for the design of the infographic used in this article.

References available on our website.

Dr Dilek Taze
Histopathology Registrar ST3
Leeds Teaching Hospitals Trust & Calderdale and Huddersfield Foundation Trust

Dr Kathryn Griffin
NIHR Clinical Lecturer in Histopathology
Leeds Teaching Hospitals Trust & Leeds Institute of Cardiovascular & Metabolic Medicine, University of Leeds

RETURN TO CONTENTS

Using digital pathology to enhance histopathology–surgery–radiology case-based reviews

Clare Verrill

Richard Colling

Saiful Miah

Tom Leslie

During the pandemic, digital pathology proved invaluable when in-person meetings were not possible. It has also now become a key part of learning and development across cancer care.

Digital pathology facilitates the sharing of histopathology whole slide images and provides the platform for enhanced clinicopathological discussions. This has become particularly relevant during the COVID-19 pandemic, which shone a spotlight on the need for digital pathology to maintain activities that were often not possible in person.[1]

Oxford University Hospitals NHS Foundation Trust is part of the PathLAKE (Pathology Image Data Lake for Analytics, Knowledge and Education) digital pathology consortium, which is one of the UK Government's Artificial Intelligence (AI) Centres of Excellence.

We achieved the milestone of scanning 100% of surgical histology workload in 2020 using the Philips IntelliSite digital pathology platform. Our lab generates over 1,500 scanned whole slide images and 1.6 Tb of data per day.

Offering learning opportunities

The potential for digital pathology to provide shared learning opportunities between histopathologists and other clinicians using the scanned slide images became apparent very quickly.[2] One particular example was the use of the platform to review the outcomes of radical prostatectomy surgery. Understanding, for instance, the exact location and context of a positive surgical margin can provide invaluable feedback to the urological surgeon, including those in training. Conversely, it can help histopathologists, as well as trainee histopathologists, to understand how different surgical techniques might be applied in different clinical scenarios to facilitate their understanding of the macroscopic and microscopic appearances of the specimens.

Improving communication

The urological surgical team in Oxford can log into the histopathology image management system and are able to review whole slide images on their cases once authorised. This means that the histopathology team have to think carefully about providing clear and unambiguous annotations on slide images for the non-pathologist to

Figure 1. The surgical, histopathology and radiology teams on a case-based review meeting.

RETURN TO CONTENTS

Ruth MacPherson

Francisco Lopez

Claudia Mercader Barrull

Mutie Raslan

RETURN TO CONTENTS

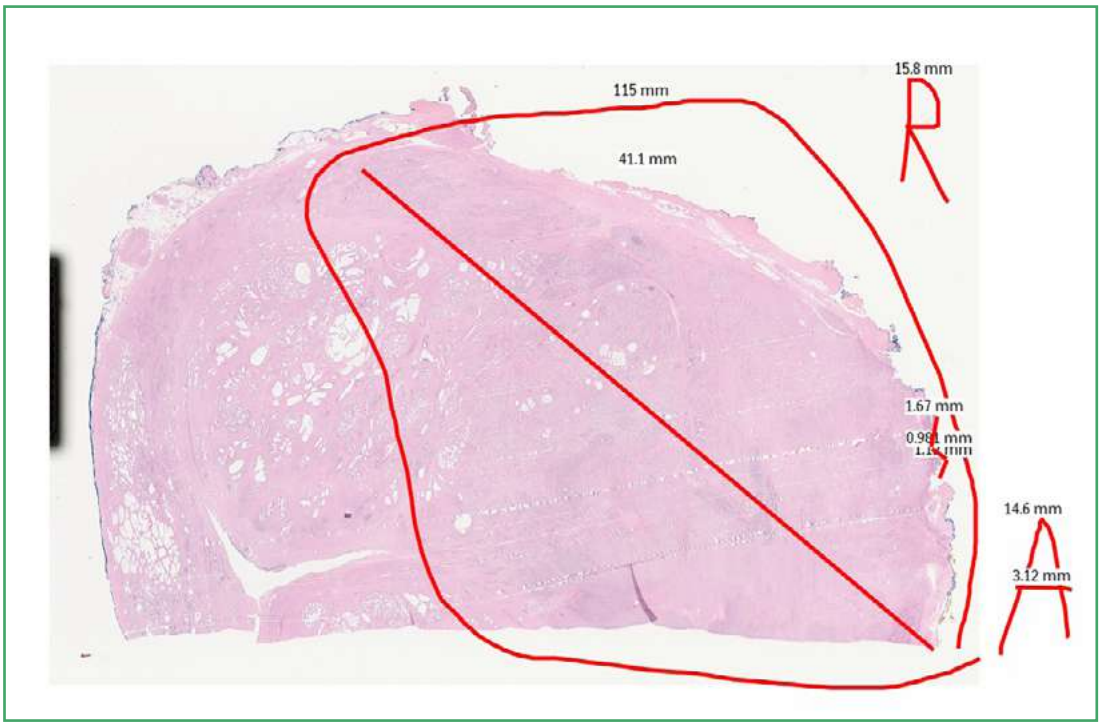


Figure 2. A radical prostatectomy case discussed during our meeting with shared learning points, including the location of a positive margin anteriorly.

understand. It is often also useful to signpost the particularly relevant slides in the report.

Facilitating feedback and development

A dedicated 'histopathology-surgery-radiology' educational review for post-surgical radical prostatectomy cases was implemented in our Trust in November 2020 to cover interesting cases with learning points. The meetings are attended by the urological surgery, histopathology and radiology teams. Approximately five to seven cases are discussed to enable sufficient opportunity for clinicopathological discussion outside of a time-pressured multidisciplinary team discussion.

During the pandemic, the meeting was held remotely over Microsoft Teams (Figure 1). With an increasingly regional service, it is important that our colleagues in our other network centres (e.g. High Wycombe and Milton Keynes) who operate in Oxford are also able to join.

Discussions cover the surgery, the pre-biopsy multiparametric MRI (mpMRI) and the histology slides and typical cases include unexpected discrepancies in tumour location and a particular focus on unexpected positive margins.[3] Figure 2 shows a radical prostatectomy case with a large anterior tumour discussed in our meeting on 29 April 2022. The circumferential margin was positive (extra-prostatic) at '11 o'clock' due to insufficient extracapsular tissue being left on the prostate anteriorly. Our normal practice of detailed, radiologist-led MRI review prior to surgery (robotic-assisted radical prostatectomy [RARP] planning meeting) to pinpoint the location of tumours and plan which areas of the prostate 'clockface' need wide dissection is intended to avoid this but is not always successful. Continuous feedback is essential to refine radiological assessment and to ensure correct adjustments to surgical technique.

The impact of digital pathology

In summary, digital pathology has significantly enhanced interactions and case-based discussion between histopathology and our surgical and radiological colleagues with shared learning opportunities for all.

The authors note that PathLAKE has received some in-kind industry investment from Philips.

References available on our website.

Clare Verrill
Associate Professor and Honorary Consultant in Cellular Pathology
Nuffield Department of Surgical Sciences, University of Oxford

Richard Colling
Senior Clinical Research Fellow and Consultant in Cellular Pathology
Nuffield Department of Surgical Sciences, University of Oxford

Saiful Miah
Consultant Urologist
Nuffield Department of Surgical Sciences, University of Oxford

Alastair Lamb

Tom Leslie
Consultant Urologist
Department of Urology, Oxford University Hospitals NHS Foundation Trust

Ruth MacPherson
Consultant Radiologist
Department of Radiology, Oxford University Hospitals NHS Foundation Trust

Francisco Lopez
Pelvic Uro-Oncology Fellow Nuffield Department of Surgical Sciences, University of Oxford

Claudia Mercader Barrull
Pelvic Uro-Oncology Fellow Nuffield Department of Surgical Sciences, University of Oxford

Mutie Raslan
Pelvic Uro-Oncology Fellow Nuffield Department of Surgical Sciences, University of Oxford

Alastair Lamb
Cancer Research UK Clinician Scientist, Honorary Consultant Urologist
Nuffield Department of Surgical Sciences, University of Oxford

Mary N Sheppard

A new national programme for genetic testing and cardiological screening of families after sudden unexpected death

Mary N Sheppard describes the development of an important national programme in England supporting detailed cardiac examination and genetic testing at autopsy with cardiological screening of families following sudden unexpected death. This will be a vital step towards prevention of further fatalities.

Sudden unexpected death (SUD) is defined as a natural, unexpected death. In witnessed cases, it is an acute event with the time to death being <1 hour, and in unwitnessed cases it is defined as a person last seen alive <24 hours before being found dead.[1] It is also labelled as sudden cardiac death (SCD), as most of the causes are cardiac. SCD is frequent in older age groups, largely due to ischaemic heart disease.[2]

In younger people, it is mainly due to sudden arrhythmogenic death syndrome (SADS), where the heart is morphologically normal but fails due to electrical abnormalities (cardiac channelopathies) and structural cardiomyopathies (CM). Both of these are mainly genetic. It is especially important that SCD in younger people is investigated with autopsy, as these genetic cardiac conditions have important implications for their families.[3–5]

Establishing a cardiac pathology reporting service

I wrote an article for the Bulletin in 2012 that set out the roadmap for the investigation of SCD in the UK. This followed a meeting of experts in the field that highlighted the many difficulties facing pathologists in such cases, in view of the genetic implications and prevention of further deaths within families. The article included guidelines for obtaining consent for tissue retention and genetic testing within the framework of the Human Tissue Act of 2004.[6] The major issues arising were:

- retention of cardiac tissue with storage and location of the retained tissue
- the appropriate tissue to be taken for genetic testing, the pathway for the genetic testing and who should pay for this
- who would arrange cardiological screening of the families.

I am glad to write now and provide an update with a very positive message.

Following this meeting, we established a nationally available, free service for prospective reporting on the cardiac pathology of SCD in collaboration with a UK charity called Cardiac Risk in the Young (CRY), funded by bereaved families. This service enables us to process hearts referred from coroners and pathologists throughout the UK and obtain fresh spleen tissue for genetic testing. Since 2013, we have built up over 7,000 cases in this database, with most cases being due to SADS and CM (Figure 1). The post-mortem genetic material has provided valuable positive results.[7,8]

Development of genomic hubs

The NHS has an increasing role in harnessing the power of genomic technology and science to improve the health of the population. In 2019,

RETURN TO CONTENTS

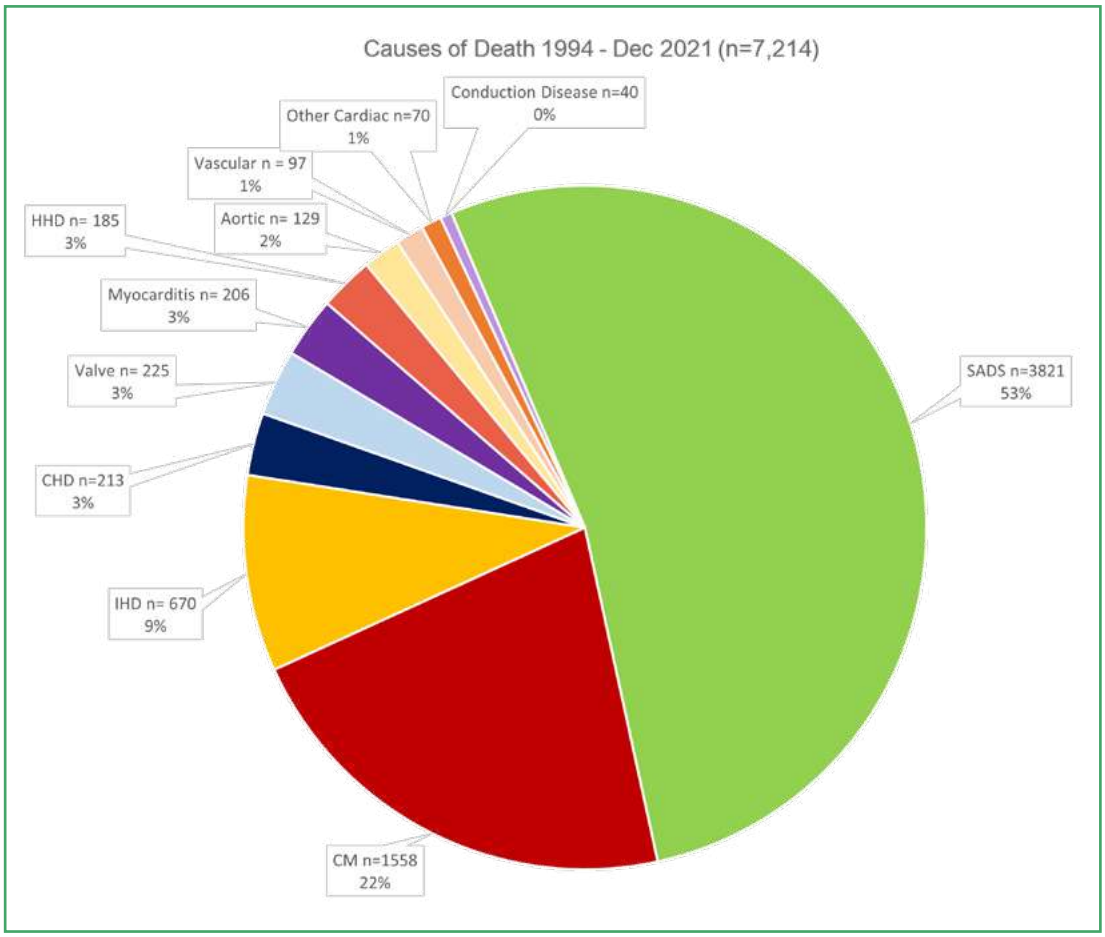


Figure 1. Causes of death identified from 1994 to 2021 in the CRY database.

an NHS document on genomics and prevention resulted in the implementation of Genetic Medical Service Alliances since 2021 to deliver a single national testing directory, covering use of all technologies from single genes to whole genome sequencing.

Most importantly, from our point of view, it established a national genomic testing directory for rare and inherited cardiac diseases, including aortopathies, vasculopathies, cardiac channelopathies and cardiomyopathies.[9,10] This testing directory led to the establishment of seven regional genomic hubs:

- Central and South Genomic Laboratory Hub, led by Birmingham Women's and Children's NHS Foundation Trust
- East Genomic Laboratory Hub, led by Cambridge University Hospitals NHS Foundation Trust
- North West Genomic Laboratory Hub, led by Manchester University NHS Foundation Trust
- North Thames Genomic Laboratory Hub, led by Great Ormond Street Hospital for Children NHS Foundation Trust
- South East Genomic Laboratory Hub, led by Guy's and St Thomas' NHS Foundation Trust
- South West Genomic Laboratory Hub, led by North Bristol NHS Trust
- North East and Yorkshire Genomic Laboratory Hub, led by the Newcastle upon Tyne Hospitals NHS Foundation Trust.

These now provide the opportunity for the systematic introduction of post-mortem genetic testing for SUD cases with possible genetic cardiac causes. The College has issued recently updated guidelines on reporting and taking of genetic material at such autopsies.[11]

A multidisciplinary approach to genetic testing

With NHS England and charities including the British Heart Foundation (BHF) and CRY, we have undertaken a pilot study to establish a multidisciplinary team of coroners, coroners' officers, pathologists, cardiologists, geneticists and genetic scientists in each of the seven pilot sites. A coordinator has been appointed in each region to direct the pathway from the pathologist, the coroner and coroner's officer as they process the retention of tissue and taking of genetic samples, through to the family and referral to the inherited cardiac conditions services within each genomic region (Figure 2).

Genetic testing will be undertaken within the Genetic Hubs once the family has been seen by a specialist cardiologist and the cardiac phenotype is established by the pathologist at autopsy. The logistics of tissue retention and sample handling for genetic testing will be supervised by the

RETURN TO CONTENTS

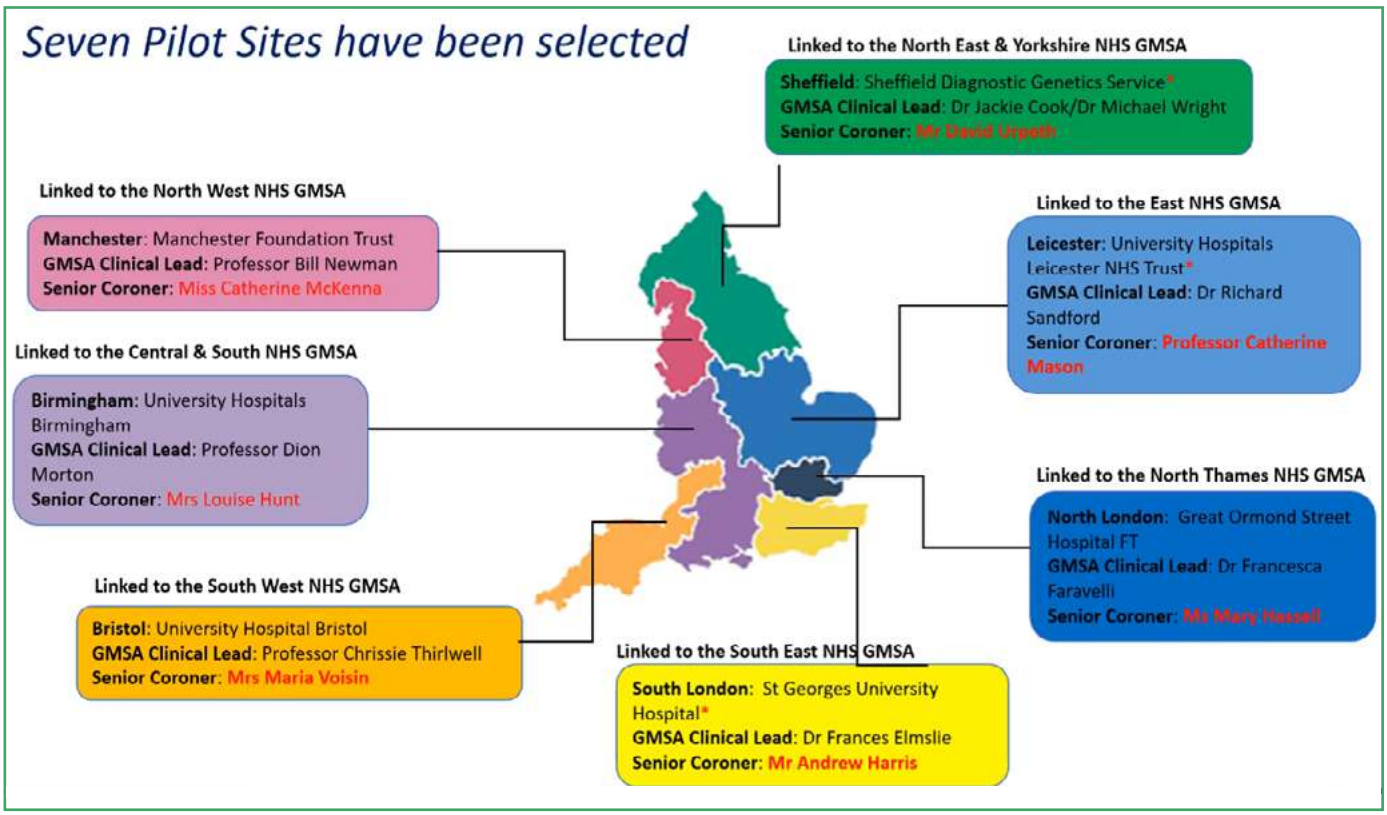


Figure 2. Locations of the seven pilot sites in each genomic region of England.

regional coordinator and will be appropriately funded. Already, cases are entering this pathway within each region. This whole endeavour has continued to progress despite the challenges of the pandemic.

The pilot study highlights the need for the expertise of specialist cardiac pathology centres.[12] It is necessary to review the cardiac cause of death, as cardiac phenotype is so important for family screening. As with oncology services, reviews are needed for especially challenging cases.[13] Yes, pathologists can get it right first time,[14] but more training is needed in cardiac pathology, as general training in autopsy does not prepare pathologists for the more challenging cardiomyopathies and congenital heart lesions.[15] We also need pathological guidelines for these entities, which we are producing with the European Association of Cardiovascular Pathology.

The autopsy rate for SUD in Europe varies widely, with the average being 43%, while genetic testing averages at 48%, which leaves a large gap.[16] This pilot study, in which there should be an autopsy rate of 100%, will yield invaluable information that will expand our knowledge of the cardiac causes of death with clinical follow-ups and genetic testing. The pathologist will be a vital part of the multidisciplinary team investigating these SUDS.

This pilot development within the NHS is a major breakthrough, as pathologists and coroners will no longer have to worry about costs and will have a coordinator to arrange the logistics and follow up in each case. This should lead to full investigations and prevention of further deaths within families, as most SCD cases, especially in the young, are genetic. We pathologists will be at the heart – literally – of this programme.

This exciting initiative would not have been possible without the support of NHS England and Dame Sue Hill, BHF Director Sir Nilesh Samani, CRY chief executive Dr Steve Cox, College President Professor Mike Osborn and Professor Elijah Behr, Chair of the National Steering Group.

References available on our website.

Mary N Sheppard
Professor of Cardiovascular Pathology
St George's Medical School, University of London

RETURN TO CONTENTS

An innovative programme by Genomics England for harnessing the power of multimodal data in cancer diagnosis and research

Emma McCargow

Dr Prabhu Arumugam

Through the NHS Genomic Medicine Service, Genomics England works with NHS England to develop a personalised, predictive healthcare solution for all. Emma McCargow, Programme Lead, and Dr Prabhu Arumugam, Director of Clinical Data and Imaging, describe the programme's successes.

Our mission is to continue refining, scaling and evolving our ability to enable others to deliver genomic healthcare and conduct genomic research.

Innovation in cancer data

At our Research Summit in May, we announced our Cancer 2.0 initiative, which is centred on the use of innovative technologies to analyse cancer data to deliver earlier and more accurate diagnoses than have previously been possible. Our ambitious goal is to build the world's biggest cancer research platform.

Central to the initiative is the use of long-read sequencing technology – the sequencing of very long strands of individual DNA without the need to slice them up – and multimodal data to support earlier and faster diagnosis of cancer.

What is exciting about long-read sequencing is its capability to reveal new information about whole regions and large structural features of the genome that were previously inaccessible to traditional sequencing. This offers insights into cancer that are not possible using other technologies.

The benefits of multimodal data

A critical component of the initiative is the use of multimodal data.

Currently, valuable data is held in a variety of formats and systems within different health disciplines (e.g. genomics, pathology and radiology, including MRI and CT scans). The multimodal project will combine these three distinct data types – medical disciplines that have traditionally been siloed and separated – alongside the clinical follow-up data from patients.

There are challenges associated with extracting meaningful clinical insights from such data, both due to the scale of the data and the complexities of comparing across data types. Artificial intelligence (AI) is well suited to exploratory analyses of such data.

Our hope is that this resource will increase our knowledge of cancer, while also providing us with a greater understanding of an individual's prognosis and their response to treatment. Simultaneously combining the genetic sequence and images of a tumour will point the way forward to the development of more effective precision drugs and therapies.

Implementing digital pathology

This would not be possible without the unprecedented programme of digitised pathology slides currently undertaken by the Leeds-based National Pathology Imaging Co-operative (NPIC). In partnership with Genomics England, NPIC is scanning all the pathology slides from participants with cancer in the 100,000 Genomes Project to create a dataset of more than 250,000 high-resolution whole slide images – the Genome-Pathology Imaging Collection (GPIC) collection.

Detailed diagnostic information from pathology reports, somatic and germline sequence data, radiology data, and longitudinal clinical data will also be included, creating a unique resource for cancer researchers. This will enable scientists to get a better understanding of cancer and open the door to improved diagnoses and treatments for cancer patients.

NPIC, led by consultant pathologist Professor Darren Treanor, is also deploying digital scanners across more than 30 NHS hospitals, covering all 29 pathology networks in the UK and two national networks in paediatrics and soft bone tissue cancers.

This will allow pathologists across the country to view and read slides digitally, share cases for second opinions and facilitate national multidisciplinary team meetings to decide the best treatment options for each patient. The days of having to post slides to colleagues for second or consensus opinions are numbered.

Digital pathology images enable the participation of patients in large-scale research projects across the country and also, when analysed with AI, offer the possibility of new diagnostic and prognostic tools, better pathology-genomic correlation and novel companion diagnostic combinations.

RETURN TO CONTENTS

The multimodal project will lay the foundations for a future world in which high-quality pathological analysis is enhanced by AI and genomics work.

Next steps and more information

NPIC is setting up bespoke training programmes and workshops for digital pathology and AI. They have launched a webinar series open to all professionals, the details of which are published on their website.

Further information about the pathology-genomics correlation project to create the GPIC is available here and the NPIC website. Data from the collaboration will be available via Genomics England over the coming months as the resource develops.

To register interest and keep up to date about the progress of the project and data availability, please contact digitalimaging@genomicsengland.co.uk.

Emma McCargow
Programme Lead – Cancer
Genomics England

Dr Prabhu Arumugam
Director of Clinical Data and Imaging, Genomics England

Chasing ghosts: using artificial intelligence for feto-maternal haemorrhage estimation

Marlene Correia

Veronika Jenei

Digital morphology offers an opportunity to harness artificial intelligence-based recognition technology pathologists in the laboratory. This article discusses the benefits of modern technology in estimating the occurrence of feto-maternal haemorrhage.

Acid elution techniques using the Kleihauer–Betke (KB) method[1] are commonly employed in transfusion laboratories to estimate feto-maternal haemorrhage (FMH) during pregnancy or post-delivery. However, this is a manual, labour-intensive technique subject to interobserver variability. FMH estimation by flow cytometry (FC) is considered the gold standard[2] but it is often only available in specialist laboratories.

The development of digital morphology and machine learning is now well used for reading peripheral blood and bone marrow smears. This article investigates the feasibility of using technology to realise potential advantages in FMH screening and quantification. In this case, the technology used was a CellaVision DC-1 Digital Morphology Analyzer (DC-1) in conjunction with a newly developed Kleihauer artificial intelligence image capturing and reading prototype software (KLAIR).

Background

Haemolytic disease of the fetus and newborn (HDFN) can occur when fetal or newborn red blood cells (RBCs) are destroyed by maternal antibodies. The most frequent cause is RhD (RhD) incompatibility, when immune anti-D from an RhD-negative mother cross the placenta and target red blood cells in an RhD-positive fetus/newborn. Maternal immune anti-D can develop following FMH due to sensitising events (such as abdominal trauma, late miscarriages or medical interventions), throughout gestation or during delivery. The RhD antigen is highly immunogenic – it only takes 0.01–0.03 ml of FMH for the isoimmunisation of the mother.[3]

In the 1960s, Stern found that sensitisation to RhD-positive blood could be prevented by administering anti-D immunoglobulin (anti-D Ig), a blood product produced from the plasma of donors with immune anti-D. Since its introduction, anti-D Ig has been highly successful in reducing the incidence of HDFN and achieving improvements to maternal and fetal health.[4]

The National Institute for Clinical Excellence (NICE) recommends that all RhD negative pregnant women, who do not have immune anti-D, should be offered additional routine prophylaxis with anti-D Ig during the third trimester of pregnancy (approximately 28 weeks), in addition to post-sensitising events.

For potentially sensitising events (PSE) from 20 weeks gestation to term, including delivery, an FMH screening test is required to detect fetal cells in the maternal circulation and, if present, to estimate the volume of FMH. This allows the calculation of the additional anti-D Ig doses required to clear the fetal cells and prevent the development

RETURN TO CONTENTS

Jennifer Davies

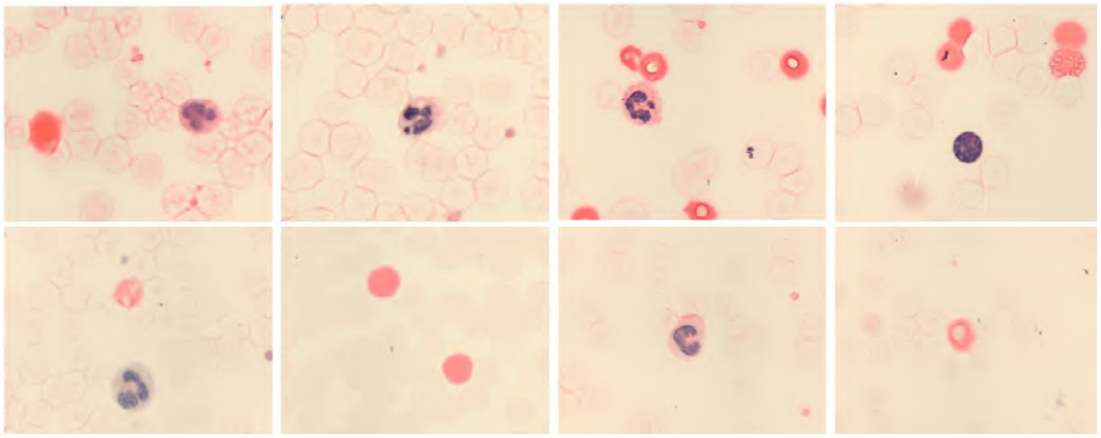


Figure 1. A selection of high-resolution images obtained on KB films stained on different days and using different blood samples. Adult red cells ('ghosts') are identified by lack of uptake of counterstain post haemoglobin elution, whereas fetal cells, containing HbF, staining pink. White cell nucleus may stain dark purple.

of immune anti-D.[5] Anti-D Ig needs to be administered within 72 hours of a PSE to be effective; delays in laboratory testing can contribute to delays in administration, putting mothers at risk.

State of affairs

Acid elution (AE) and FC are the most frequently used techniques to assess FMH. In AE techniques, an acidic reagent elutes haemoglobin (Hb) A from adult red cells without affecting fetal cells, as HbF is resistant to changes caused by low pH. Cells containing HbF are counterstained in a thin blood film, usually staining a pink colour, whereas HbA (adult) containing red cells appear as 'ghosts'. This difference allows manual microscopic cells to be counted and FMH to be estimated.

Table 1. Automated FMH results, by KLAIR, on a patient KB film with FMH bleed of 18 mL.

	Automated FMH		
	KLAIR average bleed (5 replicates)	KLAIR results distribution	KLAIR average accuracy
Patient KB film	18.38 mL	17.03–22.13 mL (SD= 2.13)	93%

FMH: Feto-maternal haemorrhage.

The KB test is inexpensive, requires no specialist equipment and is used in many laboratories as the primary screening tool for FMH.[6] However, this test has a number of shortfalls – such as the lack of standardisation in the creation of the blood film and wide inter/intraoperator variation due to manual counting of cells, which translates to a wide coefficient of variation (30–80%).[7] Protocols are often complex, laborious and time-consuming.

The recent advent of whole-slide imaging and digital image analysis has revolutionised medical laboratories, with particular emphasis on semi-automated peripheral blood film analysis. Cell location and pre-classification by automated digital platforms have improved report standardisation and have reduced review time for images, ultimately making more efficient use of the skills of experienced laboratory staff.[8]

The road so far

The first version of KLAIR was designed to obtain high-resolution images of a KB film, in which individual cells could be manually classified into three classes to begin the machine learning process: negative RBCs (adult cells), positive RBCs (fetal cells) and white blood cells (WBC). (Platelets or artefacts are not annotated and are excluded from analysis).

Prior to this feasibility study, two main technical challenges were anticipated. First, the colour of adult cells was expected to be too pale to be detected by the DC-1 camera. Secondly, the wide variation in colour could be a problem for KLAIR to overcome, preventing it from learning to classify cells accurately. It was demonstrated that the DC-1 camera could collect high-resolution images where adult and fetal cells could be identified by KLAIR (Figure 1).

Annotated and classified images were used to train a convolutional neural network (CNN) to automatically recognize and classify individual cells. These were taken from over 250 high resolution images of KB films from patient samples for discard, UK National External Quality Assessment Services (NEQAS) samples and internal quality control slides.

Successive machine learning was performed using an iterative process. Every new labelled data item obtained was reviewed. Cell classification was amended where the cells were incorrectly classified by KLAIR. The CNN was retrained using the reviewed images. This data was then used to create

RETURN TO CONTENTS

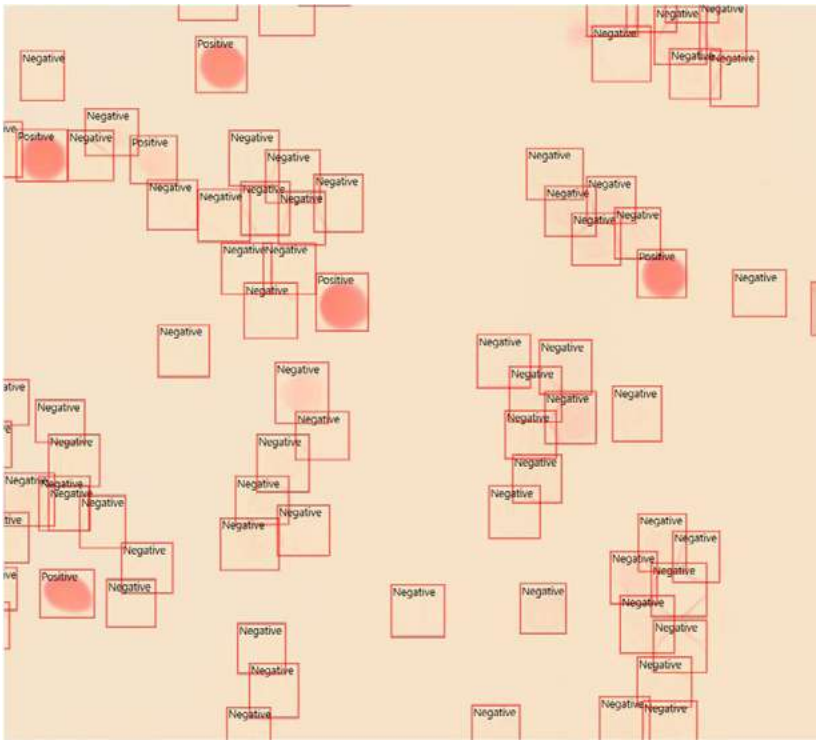


Figure 2. Example of automatic cell detection and cell classification by KLAIR's latest version, on a positive control KB film.

a new version of KLAIR, which was re-evaluated and used to obtain new data with further annotated images (Figure 2).

During this process, new functionalities were added to KLAIR, including automated calculation of the percentage of fetal cells in the maternal blood, automated FMH estimation in mL and an automated area finder (allowing the DC-1 to automatically identify the monolayer of the KB film to optimise cell counting).

What's next?

A preliminary assessment of KLAIR's performance was done, using a patient KB film, with an FC confirmed bleed of 18 mL (Table 1). Our preliminary results appear to show that KLAIR's accuracy may be superior to manual microscopy when compared to acid elution methods. A similar size bleed (18.8 ml) was reported for two samples issued by NEQAS FMH (distribution 2202), where manual microscopy accuracy was reported as 82% (Table 2).[9] Although this feasibility study seems to demonstrate that KLAIR can automatically and accurately estimate FMH bleed with no requirement for manual intervention, further work is required.

The next steps will see KLAIR's performance compared against manual FMH estimation and FC using 30 blood samples with fetal RBC concentration range of 0–6%, simulating FMH bleeds that are considered normal during uncomplicated deliveries, clinically significant FMH (›30 mL) and significant fetal bleeds (150 ml), as described in literature.[10]

This feasibility study has demonstrated the power of artificial intelligence and emerging machine learning approaches to an automated KB screening method. Automated methods allow higher number of cells per KB film to be analysed compared to manual counting, which reduces the variability of manual counts. This technique has the potential to be combined with automated slide makers, which would increase standardisation, improve the accuracy of FMH estimation and reduce delays in testing and releasing staff time. This will ultimately translate to better, faster diagnosis and improvements in patient care during pregnancy and at delivery.

References available on our website.

Marlene Correia
Specialist Biomedical Scientist
Royal Devon University Healthcare NHS Foundation Trust

Veronika Jenei
Scientific and Medical Affairs Manager
CellaVision

Jennifer Davies
Blood Transfusion Manager
Royal Devon University Healthcare NHS Foundation Trust

Table 2. Manual microscopy accuracy, as reported on a recent NEQAS FMH distribution of similar size bleed (18.8 mL)

	Estimated FMH by manual microscopy		
	Overall method median (Manual microscopy by NEQAS participants)	NEQAS participants results distribution	Manual microscopy accuracy
NEQAS sample 2202-1	22.2 mL	5.8–38.3 mL (estimated SD = 3.9)	82%
NEQAS sample 2202-2	22.2 mL	5.2–38.9 mL (estimated SD = 4.3)	82%

FMH: Feto-maternal haemorrhage.

RETURN TO CONTENTS

PROFILE: DR STEPHEN MORLEY, ASSISTANT REGISTRAR

The College's Assistant Registrar, Dr Stephen Morley, introduces himself and his approach to the role in this profile. He discusses the main issues facing the pathology workforce as well as how members can take the lead in improving the work of the College.

Why did you become Assistant Registrar?

I had not previously considered getting involved in the College, but I wanted to make changes to the way that the College represented me and other members. I feel that, if I am unhappy with a situation, then it is partly my responsibility to work to resolve this. Therefore, when the Assistant Registrar position came up, it seemed an ideal opportunity to start to try to make changes.

What does the Assistant Registrar do?

Workforce

One area of my work is supporting and representing the Workforce team – you can read about the team and the workforce cycle in an article from the July *Bulletin*. This is a very challenging area, both regarding data collection, but also taking into account the changing workforce. Non-medically trained senior staff are growing in importance and there has been a growth of the female workforce over the last few decades. There are also the possibly unforeseen effects in pension changes such as early retirement, as well as, as an example, the support of senior female staff balancing the effects of the menopause and work.

I also have responsibility for the specialty and associate specialist doctors, who are becoming increasingly important within the pathology workforce. Many colleges, including RCPath, need to review how we support these locally employed, non-consultant grade staff.

Acting as a College trustee

Another role of the Assistant Registrar is to act as a trustee for the charity, which the College is defined as. A trustee's role in a charity is to be the 'guardians of purpose', making sure that all decisions put the needs of the beneficiaries first – in this case, the College membership. They safeguard the charity's assets – both physical assets, including property, and intangible ones, such as its reputation.

> Without accurate workforce data, the College cannot lobby parliament.

As an example, the College has an investment portfolio, which the trustees must approve. At present, the trustees have made the decision not to invest in fossil fuels. But, with the very large profits and dividends of the industry, there was a recent discussion over whether the College should review this. There is a balance to be held between improving College finances (and hence not having to increase membership fees) and investing in what the trustees felt was ethically unacceptable.

RETURN TO CONTENTS

What are the challenges for the Assistant Registrar in the next few years?

As everyone is aware, the NHS workforce is struggling, even before the pandemic. Without accurate workforce data, the College cannot advocate for change. Workforce data helps the College support both trusts and the new networks in ensuring there are adequate numbers of staff, but also that these staff numbers will inevitably grow. The College needs to provide the data so that an appropriate number of specialty registrar posts, as well as clinical scientist and advanced practitioner posts, are created. This is already happening with one of the largest amounts of histopathology training numbers (including new numbers) being advertised in 2021.

There is also a move to pathology networks, and the workforce data must reflect the direction of network travel, which, in turn, is affected by the local trust situations.

The data has always been significantly retrospective and is often collected over a five-year cycle. I have been supporting the Workforce team in two aspects. We are going to be collecting data more frequently and this will likely be collected at the network level. This will have several advantages, in that the data and lobbying will be more receptive to changes over time. The other advantage is that each region employs a workforce team, so much of the work can be carried out by this team rather than the already stretched Clinical Director of Pathology or their management team. We are collaborating with NHS England/Improvement (NHSEI) and specialist bodies to ensure data collection is not replicated (and so your clinical directors and pathology management time is used more effectively), and that the same message is given by the College, NHSEI and specialist bodies.

How do you relax?

Although my trust is very supportive of my voluntary College role, I still have a whole-time equivalent consultant role as a chemical pathologist and toxicologist. However, I do have a life outside work (which makes me more effective in work). I have a passion for motorsports, and am the proud owner of a TVR Chimera 450, which I can be seen driving across Snake Pass (a beautiful driving road between Sheffield and Manchester) of an evening to blow away the cobwebs. I also literally blow away the cobwebs as a euphonium player in a local brass band, which, like driving the TVR, requires total concentration and so makes me completely forget about work for a few hours a week.

Would you recommend taking on a College role?

Most definitely! The College continues to review the services it offers to members and make improvements. Change can sometimes be slow but, by getting involved in the College, you can use your voice to push forward the changes you want to see happen.

The Academy of Royal Medical Colleges has recently sent a letter to all Trust medical directors to remind them that they are expected to release consultant staff for added-value roles and that staff should be encouraged to apply and take up roles. Now is a great time to look at what College roles are available.

The William Tong Prize: exploring the variability of the hepatitis E virus ORF2 capsid protein between genotypes 1 and 3

Becky Haywood

At this year's UK Clinical Virology Network annual conference, the William Tong Prize was awarded to Becky Haywood for her work on the hepatitis E virus capsid protein in genotypes 1 and 3. This article outlines her project looking at the variability of the HEV capsid protein.

The award was established in memory of the late William Tong who, at the time of his death in 2018, had just stepped down as Chair of the College Panel of Examiners in Virology. Family and friends of William Tong raised funds to create a prize in his name (see the article in the October 2019 *Bulletin*) to be awarded for outstanding original work in clinical virology.

Becky Haywood is a biomedical scientist working in the Blood Borne Virus Unit at the UK Health Security Agency (UKHSA). Since 2017, she has been working on her PhD part-time under the

RETURN TO CONTENTS

Sophie Gillett

supervision of Dr Samreen Ijaz and Dr David Allen with the London School of Hygiene and Tropical Medicine.

Investigating the hepatitis E virus

Background to hepatitis infection

Four major hepatitis E virus (HEV) genotypes infect humans (G1–G4); the epidemiology, clinical features, transmission route and reservoirs differ significantly according to the genotype. G1 and G2 are restricted to humans and are primarily transmitted via the faecal–oral route. G3 and G4 are zoonotic infections, infecting humans in addition to a wide range of ungulates and other mammals. Transmission to humans of G3 and G4 is linked to the consumption of raw or undercooked meat products, particularly those of porcine origin.

Modelling of HEV viraemia in blood donor data suggests that 80,000–100,000 human infections occur in England annually. While the majority of these will be acute self-limiting infections, chronic infections in immunocompromised individuals are increasingly identified. These chronic infections can be difficult to manage due to the limited treatment options available and the risk of relapse following treatment cessation.

HEV infections in England are dynamic with an increase in case numbers observed since 2010; phylogenetic analyses indicate this rise is associated with the emergence of G3 clade 2 viruses (G3 subgenotype c), which were not in common circulation prior to 2010. Prior to 2010, only G3 clade 1 viruses (G3 subtypes e and f) were seen in the UK.

Study outline

The aim of my project was to explore the variability of the HEV capsid protein in genotypes 1 and 3, which make up the vast majority of HEV infections in England and Wales, to better understand the impact of viral diversity on the antigenicity and functionality of the HEV capsid.

To characterise the genetic variability across the HEV genotypes and subtypes found in HEV infections in England and Wales, I used publicly available crystal structures for both genotype 1 and genotype 3 HEV capsid proteins as scaffolds to predict protein structure from sequence data collected from the UKHSA HEV enhanced surveillance programme. These analyses provide an opportunity to utilise this routinely collected sequence data to model specific amino acid changes and investigate the impact of this variability on the conformation of the HEV capsid protein.

I collected 722 HEV sequences generated from viruses identified between 2014–2016 for analysis; 88% were G3 sequences, with the remaining 12% being G1. In line with data from the past decade, the majority were G3c viruses. My initial analyses of the G3 sequences found that the consensus for both clade 1 and clade 2 G3 viruses were identical, bar one difference in the protein's c-terminal region. This allowed analysis of clade 1 and clade 2 viruses together and a direct comparison of G1 and G3 virus sequences. The G3 sequence alignment had much higher levels of variation compared with the G1 alignment as measured by the Shannon entropy score. However, this may have been due to the higher numbers of G3 sequences analysed.

Following translation of the nucleic acid sequence to amino acid residues, 19 amino acid differences between G1 and G3 were identified. Of these 19 differences, 11 were in the surface exposed P region, 5 in the M region and 3 in the C-terminal region of the capsid protein. When modelled onto published crystal structures, a difference in the total accessible surface area (ASA) of approximately 2,000 Å^2 was noted between the G1 and G3 protein.

Graphical plots comparing the ASAs of each individual amino acid residue were generated, and two regions of significant variance between G1 and G3 were identified: region A comprising amino acids 483–493, and region B comprising 579–591. Both were found in the surface-exposed P region.

Homology modelling using consensus sequences for G1 and G3 was performed and superimposed. Overall, the capsid protein structure is highly conserved across most of the protein monomer; however, visible differences in predicted protein structure were seen in two areas, corresponding to regions A and B.

Future outlook

Further studies are ongoing, utilising virus-like particles and cell culture techniques to investigate the impact of this variation on antibody recognition and neutralisation. It is hoped this better understanding of the antibody response to the HEV capsid will lead to improved serological assays which better reflect the viruses commonly identified in the UK. In addition, identifying neutralising antibody epitopes could open avenues to therapeutic options for the chronically infected whose choices are currently limited.

It was an honour for my work to be recognised with the William Tong Prize, especially given Dr Tong's background in bloodborne viruses. I would like to take this opportunity to thank Dr Samreen Ijaz, Dr David Allen and Dr Anna Godi for their invaluable support during my PhD.

Becky Haywood
Biomedical Scientist
UK Health Security Agency

Sophie Gillett
Consultant Virologist
UK Health Security Agency

RETURN TO CONTENTS

Dr Elizabeth Stokes' legacy celebrated with donations to the College

Professor Angharad Davies

Professor Shaheen Mehtar

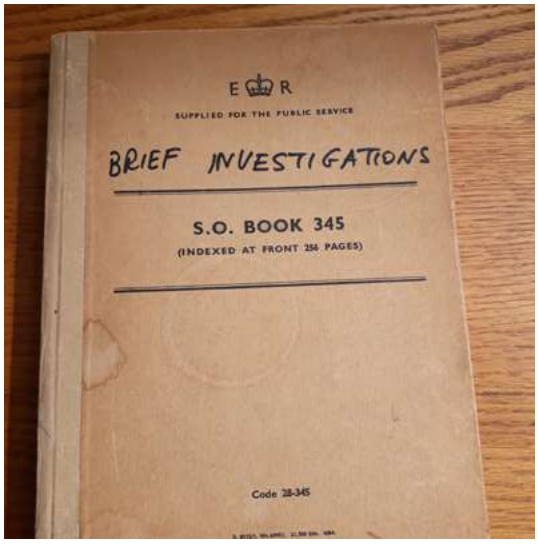
The memory of the well-known medical microbiologist, Dr Elizabeth Stokes, has been honoured with donations to the College Library of her personal lab equipment. In this article, Professor Angharad Davies and Professor Shaheen Mehtar recount Dr Stokes' contribution to the College and her field.

Dr Elizabeth Joan Stokes is a name that will be familiar to many of our medical microbiology members. An eminent clinical bacteriologist at University College Hospital London from 1946 to 1977, Dr Stokes is credited with leading the way in establishing medical microbiology as a specialty within pathology. Her eponymous technique of antibiotic susceptibility testing, the 'Stokes method', remained in use for many years and will still be remembered by many College members in the specialty.

Dr Stokes was also a Founder Fellow of the College. It was, therefore, particularly special, in the College's Diamond Jubilee year, for the College Library to receive gifts of several items that belonged to Dr Stokes: a notebook, magnifying glass, and her dissecting microscope. These were generously presented by Professor Shaheen Mehtar (the notebook and magnifying glass) and Dr Geoff Ridgway OBE (the microscope), two of Dr Stokes' last Senior Registrars.

The College would like to express its sincere thanks to Professor Shaheen Mehtar and Dr Geoff Ridgway for donating these precious items to the College library.

Professor Angharad Davies
Vice President for Learning



The laboratory notebook used in Dr Stoke's investigations.

Dr Stoke's legacy to the College

Dr Stokes was my teacher and mentor. Her passion for clinical microbiology is encompassed in this notebook titled Brief Investigations, which documents short experiments into clinical cases, such as post-transfusion septicaemia with Pseudomonas aeruginosa. Dr Stokes was meticulous in her methodology, documenting every step and painstakingly investigating samples and patient isolates until an answer was found.

Reunion of Dr Stokes' last three registrars, London 2022: Dr Geoff Ridgway OBE, Professor Shaheen Mehtar, Dr Michael Kelsey.

RETURN TO CONTENTS

Dr Stokes' magnifying glass.

One of the entries is a letter from the University of Ceylon, dated 12 April 1972, inviting her expertise to investigate antibiotic resistance in 19 strains of gram-negative bacilli. She spent months analysing the antibiotic resistance patterns and finally wrote back on 15 June 1972 with her results.

She highlighted the interesting discovery of a Klebsiella spp resistant to streptomycin and kanamycin, moderately sensitive to nalidixic acid but sensitive to gentamicin, nitrofurantoin and polymyxin.

In her must-read investigation from May 1977 titled *Campylobacter jejuni as a possible cause of enteritis*, Dr Stokes tested several growth media and atmospheres for growing C. jejuni, and sensitivity to metronidazole.

An additional gem from Dr Stoke's notebook is the final entry of the notebook from 6 February 1978 by Ms Pam Waterworth, the 'queen' of antimicrobial sensitivity testing. In this, Ms Waterworth completes the Campylobacter experiments, possibly upon Dr Stokes' retirement.

Dr Stokes' dissecting microscope.

These brief investigations make for fascinating reading and offer an early insight into antimicrobial resistance.

The magnifying glass always hung around Dr Stokes' neck as she used it to scrutinise agar plates for growth of colonies of varying sizes and to teach her registrars about colonial morphology.

It was an honour to have been given these gems by Dr Stokes. However, I feel these are better served as part of her legacy and memory at the College Library.

Professor Shaheen Mehtar
Professor Infection Control (retired)
Stellenbosch University, Cape Town

Deaths reported to Council

The deaths of the following Fellows were announced at the 9 September 2021 Council meeting. We extend our condolences to those who grieve for them.

Leonard Charles Archard, UK
Margaret Browne, UK
Timothy Bryan Hales, UK
John Masterson Hamilton, UK
Judith Alison Margaret Hilton, UK
Jonathan Richard Kerr, UK
Khee Wee Lee, UK
Geoffrey Allan Machin, Canada
Helen Morag Morris McCallum, UK
Jennifer Anne McCaughan, UK
Andries Chris Neethling, South Africa
James Shepherd, UK
Allan Trevor Willis, UK
Isaac Wilson Morkeh, UK
Andrew David Hamilton Wyllie, UK

RETURN TO CONTENTS

Consultants: new appointment offers

The following appointments have been offered and are subject to acceptance by the applicants. The lists are prepared by the College's Workforce team, on the basis of returns completed by College assessors on consultant advisory appointment committees submitted by 5 September 2022.

Please note, we receive no return following 20% of AACs. Any forms received after 5 September 2022 will be published in the next issue. If you do not take up your post or have additional information, please inform the Workforce team. Whenever you move home or job, please inform the Membership team.

Chemical pathology appointments

Region	Employing body	Base hospital	Appointee
South West	University Hospitals Bristol and Weston	across sites	Dr Eloise A Willis

Haematology appointments

Region	Employing body	Base hospital	Appointee
Kent, Surrey and Sussex	Surrey and Sussex Healthcare	East Surrey	Dr Indu M Nair
	Royal Surrey County	Royal Surrey County	Dr Matthew Cross
South London	King's	across sites	Dr Jin-Sup Shin
	Guy's and St Thomas'	Evelina	Dr Samah Babiker
	NHS Blood & Transplant and King's College Hospital	across sites	Dr Kamala Gurung

Cellular pathology appointments

Region	Employing body	Base hospital	Appointee
East of England	Bedford Hospitals	Bedford Hospital	Dr Jenish R Patel
Kent, Surrey and Sussex	Surrey and Sussex Healthcare	East Surrey	Dr Indu M Nair
South West	North Bristol	Southmead	Dr Jonathan Potts
Wales	Cardiff and Vale University Health Board	University Hospital of Wales	Dr Mohammad Reza Abdollahi
West Midlands	University Hospitals of North Midlands	across sites	Dr Lucy Green
	University Hospitals of North Midlands	across sites	Dr Eleanor Harrison
	University Hospitals of North Midlands	across sites	Dr Nour Hemali
	University Hospitals of North Midlands	across sites	Dr Vani Jayaram

Medical microbiology, infection and virology appointments

Region	Employing body	Base hospital	Appointee
North, Central and East London	Barking, Havering and Redbridge	across sites	Dr Nadia Malik
	Barts	across sites	Dr Ximena Gonzalo

RETURN TO CONTENTS

North West	Liverpool University Hospitals	across sites	Dr James Cruise
	Liverpool University Hospitals	across sites	Dr Rachel Taggart
Yorkshire and the Humber	Leeds	Leeds	Dr Anne Melhuish
Wales	NHS Wales, Cardiff & Vale University Health Board	University Hospital of Wales, Cardiff	Dr Donall Forde
	Public Health Wales NHS Trust	Hywel Dda University Health Board	Dr Harsha Perera

Clinical immunology appointments

Region	Employing body	Base hospital	Appointee
Yorkshire and the Humber	Leeds Teaching Hospitals	Leeds	Mr Daniel J Payne

Clinical virology appointments

Region	Employing body	Base hospital	Appointee
North West	Manchester University	Oxford Road Campus	Miss Emma A Davies

Helping with pathology recruitment

Job descriptions

The College's Workforce team reviews and endorses consultant-level and specialty doctor (SAS) job descriptions for medical and scientific posts across all pathology specialties for NHS Trusts, Foundation Trusts and other employing bodies.

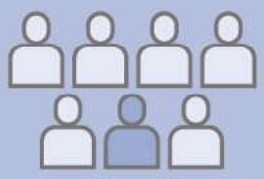
846

Number of job descriptions reviewed and endorsed over 2019 and 2020

College assessors

The Workforce team arranges for College-nominated assessors to attend interview panels (AACs) as an independent assessor to advise on the candidates' suitability for the post.

For NHS Trusts, this process contributes to the statutory framework governing the appointment of consultants.



507

Number of assessors that attended an advisory appointment committee (AAC) on behalf of the College over 2019 and 2020

If you are an NHS Trust or other employing body you can request a job description review or source a College assessor. Please contact the Workforce team at workforce@rcpath.org

RETURN TO CONTENTS

Inaugural educational afternoon for Training Programme Directors in pathology

Dr Fiona Cooke

Dr Emma Gudgin

A meeting of Training Programme Directors was recently held that allowed educators to share best practice, collaborate on various issues and explore further training opportunities across all pathology specialties. In this article, two training programme directors from the East of England share their experiences of the event.

The inaugural educational afternoon for all pathology Training Programme Directors (TPD) in the East of England was successfully held in Cambridge in May 2022. The aims of the event were to suggest good practice to other TPDs, to share peer-to-peer support and learning from other specialties, and to improve training in the East of England for trainees in pathology specialties. This first meeting was attended by the Head of the School of Pathology, who is accountable to the Deputy Postgraduate Dean and has oversight of the pathology training programmes across the region.

TPDs are responsible for the delivery of training in their particular specialty based on national standards and they help co-ordinate training opportunities within the region. Their activities include organising rotational posts for specialist registrars, induction programmes, ongoing educational activities, annual review of competency progression (ARCP) and guiding trainees in difficulty.

The COVID-19 pandemic has posed many difficulties for postgraduate training, for both trainers and trainees. This meeting was held at an ideal time for TPDs to share their experiences in managing training, as similar challenges are being faced throughout the different pathology specialties.

What did the day include?

After initial introductions, we each shared one top tip from our own specialty. These ranged from sharing online learning resources across Trusts, which was largely precipitated by COVID-19, and also improving trainees' team cohesion and peer support by holding face-to-face wellbeing breakfasts.

All pathology specialties have seen an increase in less-than-full-time (LTFT) trainees and we discussed optimising opportunities for these trainees, such as different models of accommodating LTFT trainees, including self-rostering, to ensure equitable training opportunities and service delivery compared to full-time colleagues.

We then discussed issues including administrative support, budget setting, trainees in difficulty and study leave. The Head of School was able to clarify some of our queries and explained how to raise some of our concerns.

Dr Francesca Crawley, Associate Post Graduate Dean from the East of England was invited to speak about differential attainment between international medical graduates (IMGs) and UK trained registrars. This was eye-opening, and timely with the release of deanery data on performance in postgraduate training for different groups in pathology specialties in our region.

There are ongoing discussions with the Deanery about how we can best support IMGs to fulfil their full potential. There was plenty of time for analysis of our local data with further discussion and questions.

Benefits of the meeting

The outcomes of this meeting were:

- appointment of IMG champions for both trainers and trainees, and creation of enhanced induction programme for IMGs in pathology
- establishment of trainee forums in other specialties, held every eight weeks to discuss current issues
- two specialties plan to hold a joint regional training day later this year
- continuity of wellbeing breakfasts for other specialties.

Overall, we received very positive feedback, including on the advantages of an informal face-to-face event with a relatively flexible agenda (rather than a strictly chaired Zoom session). This was focused and efficient, particularly when attendees have many pressures on their time and might not be in the position to attend general Deanery training events. Collaborative working and learning from others helps us deliver a higher standard of training, and awareness of differential attainment – in terms

RETURN TO CONTENTS

of national and regional data – will hopefully help us address some of these issues.

The event will be repeated on an annual basis but, having established relationships with the other TPDs, there will be the opportunity for informal discussions throughout the year.

Dr Fiona Cooke
Microbiology TPD, East of England

Dr Emma Gudgin
Haematology TPD, East of England

Dacie–Wilkinson lecture: a collaboration between the College and the British Society for Haematology

Established in commemoration of two eminent pathologists, this 2022 lecture was given during the College's Diamond Jubilee celebrations by Dr Wai Keong Wong, with an introduction by RCPath Registrar, Dr Lance Sandle.

Background

This lecture was first established in memory of Sir John Dacie, the fourth President of the College between 1972 and 1975. It was allocated to a conference organised by the British Society for Haematology, with the first lecture given in 2007 by Dr Trevor Baglin. The lecture has now been retitled as the Dacie–Wilkinson lecture, in memory of Dr John Wilkinson.

Sir John Dacie

Sir John Vivian Dacie, FRS (20 July 1912–12 February 2005) was born in Putney and was educated at King's College Hospital Medical School, qualifying in 1936.

After war service in the Royal Army Medical Corps, he became a senior lecturer and by 1956 was a professor at the Royal Postgraduate Medical School. He was a pioneer in the field of haemolytic anaemias. He also discovered and named Christmas disease. He was an expert in the laboratory diagnosis of the various forms of leukaemia and he founded the Leukaemia Research Fund in 1960. He was founder and editor of the British Journal of Haematology and was appointed President of the Royal Society of Medicine in 1977.

John Wilkinson

John Frederick 'Wilkie' Wilkinson FRCP FRIC (10 June 1897–13 August 1998) was born in Oldham.

In 1913, he began to study chemistry at the University of Manchester but was interrupted by war service. He graduated in 1920 with a first-class honours BSc, followed by a PhD in 1923. He then studied medicine, qualifying in 1928, and proceeded to an MD in 1931.

Experience of the effects of mustard gas in WWI suggested to him that nitrogen mustard might be effective against bone marrow cancers. During the 1940s, he pioneered research in chemotherapy for leukaemia, Hodgkin's disease and polycythaemia. He was a co-founder, with Leslie John Witts, of the British Society for Haematology (BSH).

The 2022 Dacie–Wilkinson lecture

During the College's Diamond Jubilee celebrations, this lecture was delivered in April by Dr Wai Keong Wong at the British Society for Haematology Conference in Manchester. The lecture was introduced by Dr Adele Fielding, BSH President and Dr Lance Sandle, RCPath Registrar.

Dr Wong is a consultant haematologist and is the Chief Research Information Officer at University College London Hospitals NHS Foundation Trust. He is responsible for the digital aspects of clinical trials, making routinely collected clinical data available for research and identifying opportunities for using electronic health record systems as a form of health intervention.

RETURN TO CONTENTS

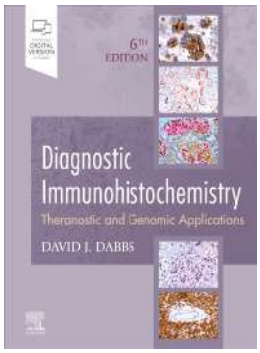
He is the co-founder of the Interoperability Education Summit and was the inaugural chair of the Chief Clinical Informatics Officer leaders' network. In 2016, he was a core member of the highly influential Wachter review into the state of NHS digitisation in secondary care. More recently, he has explored the world of data science research in the areas of machine learning in transfusion and natural language processing.

During the course of the lecture, Dr Wong shared his observations on upcoming changes in digital healthcare and the data science landscape in the NHS and made recommendations on how we can thrive as a profession in the coming years.

The full recording of this lecture will be made available via the RCPath and BSH websites.

Dr Wai Keong Wong
Chief Research Information Officer & Consultant Haematologist, University College London Hospitals NHS Foundation Trust & National Institute for Health Research

Dr Lance Sandle
Registrar



BOOK REVIEW Diagnostic Immunohistochemistry: Theranostic and Genomic Applications (6th edition)

Edited by David J Dabbs
Elsevier, 2021

£278.99, 1,000 pp, hardback
ISBN: 978-0323-72172-1

Diagnostic Immunohistochemistry: Theranostic and Genomic Applications is now in its 6th edition and comes with online access for ease of searching and portability (the second of some importance as the book comes in at 1,000 pages).

The first two chapters focus on technical aspects, quality standards and common artefacts, along with emerging technologies such as multiplex immunohistochemistry. The larger middle section discusses immunohistochemistry applications divided by organ system. Many chapters contain a subsection titled Beyond Immunohistochemistry that examines emerging diagnostic and prognostic molecular biomarkers. The book concludes with chapters on cytology, paediatric tumours, quantitative digital imaging methods and molecular techniques.

This book has healthy competition from both free reference resources (such as the well-edited Pathology Outlines website) and more authoritative subspecialty publications such as the WHO books. However, this book excels with high-quality representative images of both positive and negative staining, and side-by-side comparison with relevant H&E features.

The subspecialty chapters delve into specific discussions of when to use selected markers, with input from expert authors in the field (such as Jonathan Epstein and David Rimm). Key points for important immunohistochemical profiles and discussions of differential diagnosis are included in separate boxes for quick reference. However, a separate index for these would improve the book's usability.

A particular highlight is the chapter on Carcinoma of Unknown Primary, which has useful flowcharts regarding initial marker selection together with a comprehensive guide to the expression characteristics of the dizzying array of cytokeratin markers currently available.

There are a few negatives. Occasional images seem to have poor resolution in print. Some information appears to be included for completeness rather than immediate diagnostic utility e.g. the two-page table of risk alleles in prostate cancer would perhaps be better as an online-only appendix. The organ-orientated chapter structure leads to areas of overlap, such as germ cell tumour being covered in both mediastinal and male urogenital chapters. Indexing could be clearer in places e.g. oncocytoma has page references for both the salivary oncocytoma and renal oncocytoma under the same entry.

There is potential redundancy between the molecular techniques chapter at the end and the multiple scattered sections about testing in individual organs. Perhaps this would have been better arranged as a separate section within the book, with an overview of the different technologies followed by the case-by-case examples. This would give room to expand on the other excellent chapters, such as David Rimm's Image Analysis chapter.

A minor quibble is that the book is aimed squarely at an American audience, with multiple references to FDA approval, which are not relevant to audiences elsewhere.

Overall, I would recommend *Diagnostic Immunohistochemistry* as a useful departmental diagnostic resource that complements other reference works. It has excellent examples of positive and negative staining for trainees and consultants alike.

Dr Charles Parker
Clinical Research Training Fellow
University College London Cancer Institute

RETURN TO CONTENTS

College subscription rates for 2023

Dr Andy Boon

Daniel Ross

For 2023, the Trustee Board have recommended that member subscriptions increase by 5% and examination fees increase by 3% from 1 January. This reflects the current inflationary environment to which the College is not immune. This level of increase is not something the trustees considered lightly, and we'd like to reassure you that we are continually monitoring how we can minimise costs and obtain value for money.

The proposed rates of annual subscription to the College are published in Tables 1 and 2 below. Subscriptions are due and payable on 1 January.

The College offers several discounted rates. These include:

- UK fellows by examination automatically receive a 20% discount in their first five years of fellowship
- UK fellows earning less than £55,000 from all sources qualify for a 20% discount
- members on parental leave can receive reduced subscription rates
- the College has a scheme to consider reducing the subscriptions for members in exceptional financial hardship.

We encourage members to pay by annual direct debit or, alternatively, by monthly direct debit. From 2023, there is no additional charge for this, with amounts collected in ten equal instalments from 1 February to 1 November inclusive.

If you wish to change the way you pay your subscription to either annual or monthly direct debit, or wish to apply for a discounted membership rate as detailed above, please contact the College's Membership team by emailing membership@rcpath.org.

Dr Andy Boon
Treasurer

Daniel Ross
Chief Executive

Table 1: UK subscriptions.

	2023
Fellows	620
Fellows with income less than £55,000 per annum (2022 – £50,000 per annum)	495
Fellows by examination with less than 5 years' fellowship	495
Diplomates	310
Associates	249
Affiliates	217
Affiliate with more than 5 years' membership who are medically qualified	495
Retired with mailing	109
Medical Examiners and Medical Examiner Officers	109

RETURN TO CONTENTS

Table 2: Overseas subscriptions.

	Country band	2023
Fellows	A	328
	B	278
	C	228
	D	180
Fellows by examination with less than 5 years' fellowship	A	264
	B	224
	C	184
	D	146
Diplomates	A	237
	B	203
	C	179
	D	144
Associates	A	149
	B	126
	C	105
	D	83
Affiliates	A	119
	B	102
	C	84
	D	76
Retired with mailing	A	96
	B	84
	C	77
	D	76

College conferences

RETURN TO CONTENTS

2022 CPD-accredited events

17 October 2022
How to design and deliver pathogen genomics training for health and research professionals
26 CPD CREDITS EXTERNAL EVENT

20 October 2022
An introduction to guideline development
6 CPD CREDITS EXTERNAL EVENT

4 November 2022
Birmingham Breast Pathology Update Course - Virtual course
7 CPD CREDITS EXTERNAL EVENT

25 November 2022
Consultant Pathologist AP Update Course
LONDON - NORTH WEST LONDON 5 CPD CREDITS EXTERNAL EVENT

5 December 2022
British Society for Immunology Congress 2022
28 CPD CREDITS EXTERNAL EVENT

10 January 2023
BAUP Advanced Bladder Pathology Course
9 CPD CREDITS EXTERNAL EVENT

RCPath CPD-accredited online resources can be found here.

RETURN TO CONTENTS

Legacies

Daniel Ross

The objectives of the College are to develop and maintain high standards of pathology education, training and research; promote excellence and advance knowledge in pathology practice; increase the College's influence through a clear, coherent, professional voice; and resource the future of the College. Financially, the College aims to match activities to projected income. The College is funded from subscriptions, examinations and related fees, investment income, grants from outside bodies and charitable donations.

Bequests or legacies are always gratefully received. Leaving a gift to charity in your will is a very special way of helping to secure the future for organisations such as the Royal College of Pathologists. Legacies to the College have the added benefit of being exempt from inheritance tax.

An open legacy may be made toward the general purposes of the College. This is preferred because it allows the College to apply the funds donated where the need is greatest at the time the legacy eventually becomes available. This can be quite different from the perceived need when a will is made. However, you may legally oblige the College to spend the money in a particular area of College work or for a specific purpose by making a restricted legacy.

The College undertakes many educational initiatives. We are actively undertaking an outreach programme that spreads the awareness of pathology throughout the UK and abroad. No other UK college has committed so much time and resources to the future of our profession. This will promote the importance of pathology to the grassroots of this country through schools, colleges, hospitals and many other sites where the general public can have access to important healthcare information.

If we are to safeguard the future of our profession in the face of increasing competition from other medical and science career opportunities, it is vital that we commit ourselves to the promotion and awareness of pathology, and continue to train our young professionals to the very highest standards. This public engagement programme will require financial support from the College for years to come and we hope very much that we can build on the tremendous support you have already given and ask if you would consider leaving a legacy. Additions to your existing will can be made using a 'Form of codicil', available on our website. Alternatively, please write to us and we will be happy to post you a copy. Please note that witnesses should be present when you sign the form, but it should not be witnessed by a College member or the spouse of a College member. We recommend consulting a solicitor or qualified will writer before making a will; they should give you all the legal and tax advice that you require.

If you are considering including a legacy to the College in your will, we would very much appreciate being informed of your generous act. To inform us of your bequest or for specific advice on legacies to the College, please contact me.

Daniel Ross
Chief Executive (daniel.ross@rcpath.org)

British Division of the International Academy of Pathology

Promoting pathology through education and research

Dates for your diary

BDIAP Symposium on Upper GI Pathology

18–19 November 2022

London, UK

Further information available online

All future meetings can be found on the BDIAP events calendar
https://bdiap.org/events

RETURN TO CONTENTS

Pathological Society of Great Britain and Ireland

Pathological Society
Understanding Disease — Guiding Therapy

The Pathological Society of Great Britain and Ireland offers a wide range of grant schemes.

EDUCATION GRANTS/COMPETITION

Bursaries for undergraduate elective or vacation studies (available to Associate Undergraduate Members of the Society)	**27 February & 28 April**
Education Grant	**1 April & 1 October**
Intercalated Degree (available to Associate Undergraduate Members of the Society)	**31 March & 1 October**
Student Society Bursary Scheme (available to Associate Undergraduate Members of the Society)	**Open**
Undergraduate Essay Competition (available to Associate Undergraduate Members of the Society)	**31 August**
Jean Shanks/Pathological Society Summer Studentships	**Open**

RESEARCH GRANTS

Best Trainee Research Impact Award	**1 October**
Best Trainee Research Paper Award	**1 October**
Consultant's Pump-Priming Small Grants Scheme	**1 April & 1 October**
CRUK/Pathological Society Predoctoral Research Bursary	**25 March & September TBC**
Cuthbert Dukes Grant	**1 April**
Early Career Pathology Research Grant – Hodgkin & Leishmann	**1 April & 1 October**
Equipment Scheme	**1 April & 1 October**
International Collaborative Award	**1 October**
PhD Studentship	**1 October**
Post-Doctoral Collaborative Small Grant	**1 April & 1 October**
Trainees Collaborative Small Grant	**1 April & 1 October**
Trainees-Clinical Scientist Partnership Grant Funding Scheme	**1 October**
Trainees' Small Grants Scheme	**1 April & 1 October**
Visiting Fellowships	**1 April & 1 October**

TRAVEL GRANTS

Pathological Society Meetings Bursaries	**31 May & 31 December**
Pathological Society Meeting Bursaries for Undergraduates	**31 May & 31 December**
Travel & Conference Bursaries	**Open**

JEAN SHANKS/PATHOLOGICAL SOCIETY (JSPS) RESEARCH GRANTS

Clinical Academic Research Partnership (CARP)	**1 April & 1 October**
Clinical Lecturer Grant	**1 April & 1 October**
Clinical Lecturer Support Grant	**1 April & 1 October**
Clinical PhD Fellowship	**1 April & 1 October**
Intermediate Research Fellowship	**1 April & 1 October**
Pre-Doctoral Research Bursary	**1 April & 1 October**

OTHER GRANTS

Open Scheme	**1 March, 1 June, 1 September & 1 December**
Public Engagement	**1 March, 1 June, 1 September & 1 December**

Full details are available on our website: www.pathsoc.org or from:
Lydia Ivnik, Pathological Society of Great Britain and Ireland. E: operationsmgr@pathsoc.org
5th Joint Winter Meeting of the Pathological Society & The Royal Society of Medicine
31 January–2 February 2023

www.pathsoc.org

Events @ No 6 are delighted to offer a range of services to members of the Royal College of Pathologists. We are an integral part of the team at 6 Alie Street, providing a bespoke catering, event management and reception services.

Members and associates of the College are provided with an **exclusive 20% discount** on venue hire bookings. We would be pleased to discuss how we can provide for your personal and professional meetings and events.

The state of the art facilities provide an ideal environment for meetings with room capacity ranging up to 210 for lectures with ample break-out space for larger conferences. The six different function rooms also mean that any style of event can be held at 6 Alie Street to suit your requirements, whether it's an academic webinar, team away day, filming, fine dining, private celebrations or special events.

Visit **www.eventsatno6.com** for more information or to arrange a show round please contact our dedicated events team on **020 7451 6705** or **email sales@eventsatno6.com.**

We look forward to welcoming you to Events @ No 6.