Oxford Medicine

THE MAGAZINE OF THE OXFORD MEDICAL ALUMNI

Oxford Medical Alumni

UNIVERSITY OF OXFORD

Spring/Summer 2021

Derek Hockaday - 70 years of Oxford Medicine

Honours for Oxford Scientists and Clinicians

Vaccine-Hesitansiology

Double Blades for Osler Rowers

Pictured: Dr Peggy Frith as Dean of Degrees © Robin Frith

Oxford Medical Alumni Update

Oxford Medical Alumni (OMA) promotes good fellowship amongst Oxford Medical Sciences alumni, supports regular meetings in Oxford, and elsewhere, for continued learning, exchange of ideas, networking and socialising.

EVENTS AND REUNIONS

10th/11th: Saturday 07 August 2021 at St Hilda's College for those qualifying in 2010 and 2011

20th/21st: Saturday 02 October 2021 at Pembroke College for those qualifying in 2000 and 2001

30th/31st: Saturday 24 July 2021 at Trinity College for those qualifying in 1990 and 1991

40th/41st: Saturday 31 July 2021 at Balliol College for those qualifying 1980 and 1981

50th/51st: Saturday 11 September 2021 at Balliol College for those qualifying in 1970 and 1971

60th plus: Friday 17th September 2021 at Magdalen College for those who matriculated in 1960 or before, plus those who joined the clinical school in 1964 or earlier

To book, go to: **www.medsci.ox.ac.uk/get-involved/alumni/events-and-reunions/oxford-medical-school-reunions**

BM BCH GRADUATION CEREMONY SATURDAY 10 JULY

We congratulate all our newly qualified doctors. We wish you every success in your future careers and welcome you into the alumni fold. Stay in touch. We look forward to hearing from you.

CAREER ADVICE FOR JUNIOR DOCTORS

OMA recognises the challenges facing young doctors, some of whom are seeking inspiration and advice on their future careers. We feel OMA could play a role in facilitating informal relationships around career advice. If you feel you can help, please contact Dr Will Seligman (seligmanw@gmail.com). We are particularly looking for Consultants, GPs and senior trainees who qualified between 1990 and 2010 and are up-to-date with training programs and consultant recruitment.

RECONNECTING WITH FRIENDS AND COLLEAGUES

If you would like to reconnect with friends and colleagues you have lost contact with over the years, please email us at **oma@medsci.ox.ac.uk** and we will try our best to help.

MEETING MINDS, APRIL 2021

The University of Oxford created the virtual opportunity for alumni around the world to come together and experience an array of exciting and innovative talks, with speakers sharing their experiences and expertise across a diverse range of topics. The lecture series can be accessed online: **www.alumni.ox.ac.uk/meeting-minds**. You will need to create a My Oxford Online account in order to see them (they're behind a firewall) accessed via our website: **www.alumni.ox.ac.uk/my-oxford/my-oxford-online**

RECOLLECTING OXFORD MEDICINE

By the autumn, you should be able to enjoy the first 50 interviews in the Recollecting Oxford Medicine series. This project collects an oral history of Oxford Medicine from the 1940s onwards through face-to-face interviews and was inspired by Peggy Frith. Derek Hockaday's hard work, and skilful interviewing over that past 14 years, has produced this unique collection: **www.podcasts.ox.ac.uk/series/recollecting-oxford-medicine-oral-histories**

OXFORD MEDICAL LECTURE CLUB

The Oxford Medical Lecture Club, normally held at Osler House (John Radcliffe site), invites distinguished, entertaining, and interesting speakers to talk about their speciality and the latest developments in clinical and scientific research. Last year, the lecture series were held on Zoom and should resume in person in July 2021.

Future speakers:

Monday 26 July 2021: Professor Sir Adrian Hill 'Malaria Vaccines'

Monday 27 September 2021: Professor Paul Klenerman 'Immune Responses to Viral Infections'

Monday 25 October 2021: Professor Daniel Freeman 'Virtual Reality for the Treatment of Mental Health'

Monday 29 November 2021: Professor Sir Simon Wessely

If you are interested to receive notifications of the meetings, please contact **oma@medsci.ox.ac.uk**.

CONTRIBUTIONS TO *OXFORD MEDICINE*

We welcome your contributions to future editions of *Oxford Medicine* - clinical, scientific, creative, reflective, humorous, prose or poetry. We want to represent the full spectrum of alumni young and old, near and far.

MEMBERS OF OMA ADVISORY BOARD (OMAAB)

Dr Lyn Williamson - President OMA; Dr Roger Bodley – Honorary Treasurer; Professor John Morris, Professor Sir John Bell, Professor Gavin Screaton, Dr Catherine Swales, Dr David McCartney, Ms Christine Fairchild, Professor John Stein, Dr Tim Littlewood, Dr Kevin Windebank, Professor Denise Lievesley, Dr William Seligman, Dr Shing (Tom) Law, Dr Zoi Alexopoulou.

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President's Piece

Dr Lyn Williamson
OMA President

Welcome to the summer edition of *Oxford Medicine* featuring contributions from the collective hive mind of eight decades of Oxford Medic Alumni.

Derek Hockaday, much respected clinician and teacher, at nearly 92, takes us on his entertaining journey from life before the NHS, through the early expansion of the clinical school and medical scientific research in Oxford. The Recollecting Oxford Medicine interviews with Jean Smellie and John Spalding start in a time of war and pestilence, when medical students had to act up as doctors, St Hugh's College was a neurosurgery hospital, and polio was life-threatening and endemic. Plus ça change...

Geoff Pasvol takes up the narrative, recalling how David Weatherall and John Ledingham helped shape Oxford into the world-class clinical school and a centre for scientific research, and David Warrell set up centres for tropical diseases and malaria research. Enjoy these delightful, un-edited, first-hand accounts of two generations of Oxford medical history - the foundations upon which current clinical and scientific excellence have been built.

Congratulations to many of our scientists and clinicians who recently received honours and prizes. We particularly congratulate Sir Adrian Hill for his work on malaria vaccination and look forward to his lecture in July to the Oxford Medical Lecture Club.

OMA identical twins, Dan and Will Carroll, present contrasting clinical updates from opposite sides of the world. They join clinicians and scientists who update us on work that progressed despite the pandemic or was accelerated by it.

We pay our respects to our colleagues who died this year, particularly to David Weir, respiratory physician, who sadly died from Covid in December 2020, just days before start of the vaccination program. It is a poignant paradox that vaccine hesitancy is one of the biggest challenges we currently face, even amongst young clinicians and healthcare workers. Lisa Webber and Neil Snowise tackle the problem, acknowledging that presenting people with compelling data is not enough. We need to learn new and different techniques to compete in this arena.

Making time for creativity keeps many of us happy, healthy and functioning as good doctors. Our selection of OMA creativity includes rainy day poetry, wildlife photography before work, crossword writing after work, doodles on histopathology slide box during work and inventing a new method of violin making from dried seaweed!

The medical students play out this edition, leading us 'from the smog filled 20th Century, to a brighter, greener future... a land of positivity.' Osler Rowers came back on top form as promised, gaining double blades summer bumps! Hannah Chase and fellow students successfully campaigned for the new Sustainable Medicine Module which now weaves environmental issues throughout the curriculum. Not a moment too soon, given that hospitals are carbon footprint hot-spots. Catherine Swales, Director of Clinical Studies, has the Coda. Her prose reads like poetry, so savour every cadence from her audacity of hope to the final adieu!

COVID-19 Vaccines & SARS-CoV-2 Variants

Professor Charles Bangham
(1977 Lincoln College), Professor of Immunology & Co-Director, Institute of Infectious Diseases, Imperial College London

The success of the development and use of the vaccines against COVID-19 has been nothing short of astonishing: in little over five months, more than 1.5 billion people globally have had at least one dose of the existing vaccines, which are remarkably effective, and more vaccines are under development. The existing vaccines give a useful degree of protection against severe disease – hospitalization and death - even from the virus variants that have emerged.

The term 'variant' here can be misleading. The reason is that, like all viruses with an RNA genome, SARS-CoV-2 accumulates mutations frequently: on average it acquires a new mutation about every two or three weeks. Several thousand variants of the virus have already been described (only a small fraction of the actual number that have been generated globally), and this genetic variation has made possible detailed molecular epidemiology.

However, the great majority of new mutations don't affect behaviour of the virus; that is, they don't alter its infectiousness or the severity of the disease. Only a few mutations do matter – the so-called variants of concern. These mutations mostly lie in the receptor-binding domain (RBD) of the spike protein, the domain that binds the ACE2 receptor on the cell surface that allows the virus to enter the cell. The existing mutations in the RBD have almost certainly been positively selected for high infectiousness (the affinity of binding to the receptor is higher): it is unlikely that immune escape has been a significant selection force in the evolution of the virus to date.The possibility of immune selection is interesting and important, but there is good agreement that the overwhelming driving force in SARS-CoV-2 evolution to date is selection for rapid spread, not escape from immunity induced by vaccines or natural infection. It has been widely assumed that immune escape has already been a problem, but not only is there virtually no evidence of it, a priori one wouldn't expect it to be a big force now. But it might become so in the future. So, the main difference between these and the other circulating strains is that they are more infectious: in general, they don't seem to cause more severe disease. And the virus does not have an unlimited capacity to mutate, especially in the parts of the protein that directly affect its behaviour, such as the RBD, because some mutations will impair its function and so will be counter-selected.

Therefore, at present it seems likely that a future vaccine that contains a handful of key variants of SARS-CoV-2 will be able to give good protection against the great majority of variant viruses. Vaccines that contain a mixture of variant sequences have been in use for many years, with enormous success, for example against the pneumococcus. What is less certain is how often revaccination might become necessary, because we don't yet know how long effective immunity lasts against this virus.

Preliminary results have been reported from clinical trials in the UK[1] and Spain[2] in which volunteers received the Oxford/AstraZeneca vaccine as the first dose and the Pfizer mRNA vaccine for the second dose. The mRNA vaccine boost gave more side effects than boosting with a second dose of the Oxford/AstraZeneca vaccine, but these side-effects – such as headache, lethargy, sore arm – were mild and short-lived. Importantly, the mRNA second dose was highly effective in boosting the titre of antibodies to the coronavirus; the boosted T cell response will also play a critical part in protection.

Vaccine-induced thrombotic thrombocytopenia (VITT)

It is now clear that around one to three people in 250,000 have a potentially serious thrombotic event between one and three weeks after receiving one of the adenovirus-based COVID-19 vaccines. Nearly all the reported cases have occurred after the first dose. Most early cases were described in females, but reliable estimates of the sex ratio of the condition have not yet been made.

The paradoxical association of thrombosis with thrombocytopenia has a close precedent in heparin-induced thrombocytopenia (HIT). Heparin can form a complex with a molecule (PF4) produced by platelets, and in rare individuals this complex elicits antibodies which then aggregate platelets, forming a clot and depleting the platelets in the circulation. It appears that a similar rare series of events can be triggered by the adenovirus-based COVID-19 vaccines – the Oxford AstraZeneca and the Janssen/Johnson and Johnson vaccines. If the thrombosis is detected at an early stage, progression can be inhibited by administering intravenous immunoglobulin, which blocks the adverse effects of the pathogenic antibodies by saturating the Fc receptors on the platelets.

At present, we don't know how to predict who will get these rare reactions to either heparin or the COVID-19 vaccines. Since COVID-19 itself carries a well-recognized risk of serious thrombotic complications, the decision whether to recommend an adenovirus-based vaccine or an mRNA vaccine in a particular instance depends on the person's age and health and the current incidence of the infection.

Long Covid

It is widely recognized that somewhere between one in five and one in 20 people who develop COVID-19 will go on to develop symptoms that last for more than three months: this has become known as Long Covid. In some cases, the symptoms of Long Covid are seriously disabling, for example myocarditis or neurological symptoms. The condition was

discussed in the December 2020 issue of *Oxford Medicine*, and a fuller account is given in ref. three. Long Covid is still very little understood and very difficult to treat, and intense research is now under way on the pathogenesis of the condition. There are intriguing recent indications, albeit preliminary, that fragments of SARS-CoV-2 can persist long after the initial infection, either in protein form[4] or RNA[5], although live infectious virus has been cleared. Much further work is needed to test the possibility that these persistent remains of the virus are responsible for the syndrome.

There are anecdotal reports that vaccination can improve the symptoms of Long Covid, but there are also reports that symptoms worsen after vaccination in some people. It is not yet clear whether there is a genuine causal effect in either direction.

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Vaccinehesitansiology: The reproductive concerns

Dr Lisa Webber *(1985 Somerville College),Consultant Gynaecologist and Subspecialist in Reproductive Medicine, Imperial College Healthcare NHS Trust, London. Since December 2020, Dr Webber has been supporting the Trust's vaccination programme for frontline health and social care workers.*

With frightening prescience in 2019, the WHO named high threat pathogens, including Severe Acute Respiratory Syndrome (SARS), and vaccine hesitancy as two of ten major risks to global health[1]. Vaccine hesitancy is complex and represents the end point of a multitude of different influences and beliefs. The WHO defines vaccine hesitancy as "delay in acceptance or refusal of safe vaccines despite availability of vaccine services". Fears about vaccines affecting fertility are longstanding and can be linked to political concerns that governments – the providers of vaccines – are using them for subversive population control. These are not outlandish fears as both China and India have run state-enforced population control measures within the last generation. However, Bill Gates's involvement in public health with support of both vaccinations and population control as separate means to improve global health with the aims of reducing CO_2 emissions, poverty and unrest have been misunderstood by some, and are (mis-) quoted as reasons to reject a COVID-19 vaccine. There are also more specific fears surrounding the acceptance of a vaccine by people actively trying for pregnancy. Most people know that medication should be minimised or adjusted during pregnancy preparation, and that certain lifestyle changes are advised, such as reducing or stopping intake of alcohol, cigarettes and caffeine. There is awareness that first trimester miscarriage is common, although the role of external influences in the causation of miscarriage is considerably smaller than most expect (aneuploidy is the main reason). Fetal development can be adversely affected by drugs taken during those early weeks and this is highlighted in patient information leaflets accompanying medicines, both prescribed and over-the-counter. The horrors of the limb development abnormalities caused by the prescribing of thalidomide as a treatment for hyperemesis in pregnancy quite correctly cast a long shadow.

Experience from the vaccination programme for frontline healthcare workers (group two in the JCVI priority list) may provide insight into the vaccine hesitancy we can expect now that people of reproductive age have recently been invited for their first dose of a COVID-19 vaccine. Fertility concerns are likely to be a very significant reason for vaccine hesitancy in this young group. Explicit safety data on COVID-19 vaccines are limited for both pregnancy and fertility, although co-ordinated efforts to capture and publish outcomes for those vaccinated in pregnancy are underway with pregnant recipients identified in v-safe in America and NIMS in the UK. However, there are pregnancy safety data for a number of other non-live vaccines: influenza, tetanus, diphtheria, pertussis and poliomyelitis vaccines[2]. Vaccination against influenza and pertussis in any trimester has been routinely recommended in pregnancy for some years.

> *"...no vaccine live or non-live has ever resulted in reduced fertility..*

As for all new medicines, COVID-19 vaccines have been tested in animals, rats in this case, and there have been no adverse effects on fertility, pregnancy or pups' development (2). Concerns have circulated online that COVID-19 antibodies could attack the placenta but this has been disproved with in vitro experiments using convalescent serum[3]. Pregnancy outcomes are the same for those who have received an mRNA vaccine in pregnancy as background populations, although the numbers who received a vaccine immediately before pregnancy or in the first trimester are small in the published cohort (827 completed pregnancies)[4]. The JCVI now recommends that pregnant people in the UK should be offered an mRNA vaccine based on the American

experience as there were no obvious safety concerns. As of 17 May 2021, the v-safe database recorded that 114 thousand people in the USA had received an mRNA COVID-19 vaccine in pregnancy[5].

COVID-19, on the other hand, can have significant adverse effects on pregnant women and the fetus. Emerging data indicates that pregnant women are more likely to be affected with severe disease and twice as likely to be critically ill or die, especially if they are infected in the third trimester. If severe illness occur, the risk of pre-term delivery is increased by a factor of three[6]. Vertical transmission may occur and SARS-CoV-2 can infect the placenta. The risk of stillbirth is twice as high as in unaffected pregnancies.

No live or non-live vaccine has ever resulted in reduced fertility, and one could argue that any serious illness can indirectly, or directly as in the case of cervical cancer. Smallpox was successfully eradicated with a global vaccination programme started in 1959. Polio is close to being eradicated after effective vaccines were developed in the 1950s. WHO confidence in the long-term safety of vaccines is so high that governments are directed to have programmes to vaccinate all infants, children and adolescents against a number of transmissible diseases. The COVID-19 vaccines are the first to use mRNA as a vector for presenting an antigen, and the components of the vaccine are gone within hours of injection. Chimpanzee adenovirus vectors have had clinical use before, albeit limited, but there is no plausible reason to believe that any vaccine vector would have an effect on fertility.

As doctors, we are used to discussing the risks and benefits of any treatment when providing informed consent. The discussion with people of reproductive age, whether trying to conceive currently or planning for the future, should be straightforward as there is no reason why fertility would be affected by vaccination. There is no need to interrupt trying to conceive for COVID-19 vaccination. The conversation is more nuanced for those who are pregnant, as the safety evidence for the vaccines is still limited but data about the adverse effects of the disease in pregnancy is mounting. The vaccines are effective against serious disease caused by the virus variants that have evolved to date and seem to be as effective when administered in pregnancy. The Royal College of Obstetricians & Gynaecologists (RCOG) has produced a number of resources to help pregnant people and healthcare professionals, including a decision aid[7]. The British Fertility Society (BFS) with the Association of Reproductive & Clinical Scientists (ARCS) published FAQs for people with fertility concerns[8].

But the incidence of pregnancy is small compared to the desire for a future child. Doctors of any grade or specialty need to be prepared to reassure our young patients that there are no fertility concerns associated with COVID-19 vaccines. We should not shy from asking our patients if they have been vaccinated. Doctors are influencers, not just for our patients but for those around us and we all need to step up and help deliver a high level of vaccine uptake in the young population for the protection of everyone and as our contribution to the global fight to escape from this dreadful pandemic.

Dr Webber gave a lecture on vaccinehesitansiology to the OMA Lecture Club in May 2021. This can be watched on our YouTube channel, which is: bit.ly/OMA-WebberBangham

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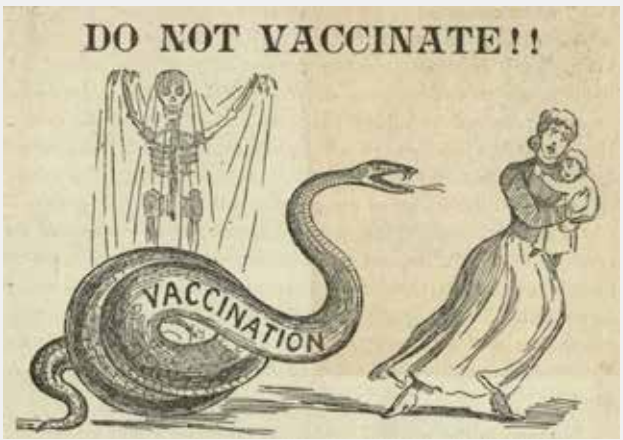


Anti-vaxx propoganda has always been eye-catching and emotive. These 19th Century examples target women's vulnerablities and deep-seated fears about fertility, child protection and beauty.

Jenner and the Antivaxxers

Dr Neil Snowise
(1974 Corpus Christi College), Visiting Senior Lecturer, Institute of Pharmaceutical Science, Faculty of Life Sciences and Medicine, King's College London

The main ray of hope shining through the gloom of the COVID-19 pandemic has been the rapid development and success of several vaccines, which are now contributing to a significant decrease in COVID-19 transmission, illness and mortality. However, the anti-vaxxers have been increasingly active, spreading a variety of conspiracy theories, including assertions that the vaccine will change your DNA, insert a micro-chip, affect your fertility and other misinformation[1]. In addition, some have vaccine hesitancy with concerns about safety, many of whom are in the BAME communities, who need the most protection because their mortality is highest. Overall, there is a significant minority who may not wish to be vaccinated, despite the historical success of vaccines in reducing many communicable diseases.

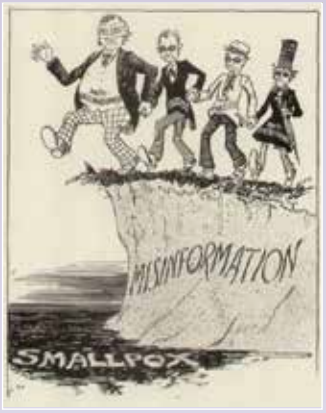
This opposition isn't new. Edward Jenner (1749 - 1823) is well-known for developing a vaccine against smallpox[2]. A GP in Gloucestershire, he observed that local milkmaids who had contracted cowpox, a mild illness related to variola virus, the smallpox virus, were protected from catching smallpox. Subsequently, in 1796, he demonstrated that vaccinating healthy subjects with cowpox offered protection from natural smallpox disease.

At one stage, smallpox was the single biggest cause of death in Europe, killing 400,000 people every year. Within five years, Jenner's discovery was being used across Europe and a decade later it had gone global. Smallpox deaths in London fell significantly. However, aggressive opposition arrived quickly from various angles - sanitary, religious, scientific and political, leading to a long battle between the authorities and an often sceptical, untrusting public[3]. Some of the clergy believed that the vaccine was "unchristian" because it derived from animals. Others believed that diseases resulted from decaying matter and were not convinced that viruses existed.

In 1840, the Vaccination Act made vaccinations free. In 1853, a new Vaccination Act required mandatory vaccination for all infants, backed by fines and even imprisonment. This legislation was not popular and triggered the first formal, organised opposition to vaccination.

While riots flared in some towns, there was also more restrained opposition in the form of anti-vaccination leagues. For an increasingly literate population, pamphlets were produced with titles like "Vaccination: its fallacies and evils", "Vaccination, a Curse" and the suitably Gothic "Horrors of Vaccination"[3].

The Leicester Anti-Vaccination League was set up in 1869 but the approach that would be praised by those opposed to vaccination came in 1877, ironically enough, from the medical establishment. The city medical examiner made it compulsory to report cases of smallpox. He would then isolate the patient, quarantine family and disinfect - and sometimes burn - belongings. Originally designed to work alongside vaccination, the League promoted it as an alternative and the "Leicester method" sparked growing defiance.



Pro-vaccination satire preaches to the converted but may not reach the vaccine hesitant.

In 1898, a new Vaccination Act introduced a clause allowing people to opt out for moral reasons - the first time "conscientious objection" was recognised in UK law.

As the use of vaccines spread - along with improved sanitation - smallpox was pushed out of Europe and North America. The World Health Organization finally declared in 1980, after an international eradication programme, that the world was rid of smallpox. This event was almost two centuries after Jenner hoped that vaccination could annihilate smallpox.

Jenner's pioneering work led to a long-standing remarkable reduction in morbidity and mortality from numerous communicable diseases, as we now appreciate. Recognition of the importance of vaccination was slower in Britain than many other countries. However, a statue was commissioned of Jenner and a site in prestigious Trafalgar Square was secured, with permission from Queen Victoria[4]. In 1858, her consort Prince Albert, a keen advocate of vaccination, presided over an inaugural occasion in the nearby Royal College of Physicians.

> *"...we need to focus on those with vaccine hesitancy, who have legitimate concerns, and ensure that the science is communicated in a positive, compelling and effective way..."*

Unfortunately, the value of vaccination was not fully appreciated. Jenner did not stay in Trafalgar Square long, as many thought it inappropriate to have a nonmilitary figure in a location which celebrated Britain's military success. Saving countless lives worldwide did not compare well with the

lives of military heroes. *The Times* supported his removal and it was demanded in parliament. His last hope and main supporter, Prince Albert, died in 1861. A year later, his statue was banished from Trafalgar Square and removed to Kensington Gardens, where it has remained for over 150 years.

Jenner's legacy is a world where we are able to prevent many infectious diseases by effective vaccination programmes. But we can also learn from history that there has always been opposition to vaccination and that we need to address this.

For much too long, the pro-vaccine groups have been reactive and reticent; they have assumed that science can speak for itself. That has not worked[1]. We need to focus on those with vaccine hesitancy, who have legitimate concerns and ensure that the science is communicated in a positive, compelling and effective way.

Information must also provide cultural competence to provide this information to people with diverse views and beliefs[5]. As we know, this is not an easy task and can be particularly challenging for some minority groups, where trust, credibility and transparency can help to build confidence[6].

Let's hope that we can learn from history and make the most of Jenner's legacy to combat COVID-19 and future diseases.

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Edward Jenner's statue was banished from Trafalgar Square after just three years (1858-61). Saving countless lives world-wide did not compare with military heroes.

A Jabbering Wreck

Dr Tim Crossley *(1974 St Edmund Hall), retired London General Practitioner*

The Pfizer shot, Waitrose to AZ's Lidl, is an easy sell. If the patient has made it to the vaccine centre, they are not anti-vax. However, they may well have misgivings as it is only then that they discover which they will have, and for every punter who prefers the Oxford vaccine there are a dozen who would rather go with the pricey option. It cannot be denied the latter has had better PR.

"How do you decide which vaccine to give people?" we get asked. The answer, for the over 40s, of course is the same way we decide what's for tea tonight. It's whatever we've got in the fridge. The randomness of this system makes patients feel they are not being picked on. One hundred and fifty patients a day, at around four minutes each, translates to 90 seconds for most and 15 minutes for the odd one who wants to discuss it at length, or who keels over. This is not super-compressed consultation skills, it is the Amazon warehouse method with the occasional complex order to fill. If you slow too much, the waiting area fills and we build up a covid-safe queue in the street. And still customer satisfaction is high! I tell them to thank scientists and the NHS, not politicians, but they don't.

Needle hesitancy occurs more than vaccine scepticism. And speed can be an asset here, though I was so fast with one nervous lady, of French origin, that she was unconvinced she'd had it. Showing her an empty syringe was only partially effective. I said she must trust me, which didn't work either. It was the Pfizer; the sore arm later would be her reassurance.

Working at this pace, one has a spiel, a kind of verbal macro spews out each time. A few basic questions about recent infections, and for younger people a question about pregnancy. I was rattling through this list, and turned my back to the patient to draw up the nectar, and raised the issue. "Is there any chance of pregnancy?" The response, "No. I'm a man." Fortunately, it was a Pfizer day.

Right Place, Right Time

Dr Steve Lockhart *(1977 New College), Vice President and Head of Europe and Asia-Pacific Vaccine Clinical Research and Development (VCRD) at Pfizer*

When I qualified from Oxford over 40 years ago, I had no clear plan beyond getting my MRCP, a vague interest in research and a wish to work in other parts of the country. Six years later, having worked in Glasgow (my first published research project), Edinburgh (MRCP), the Midlands (more publications) and London (got married and gave up my wanderlust), I thought I would try out pharmaceutical industry R&D, having been impressed by some trials I had been involved in and excited by a generation of new medicines, notably Captopril and Omeprazole.

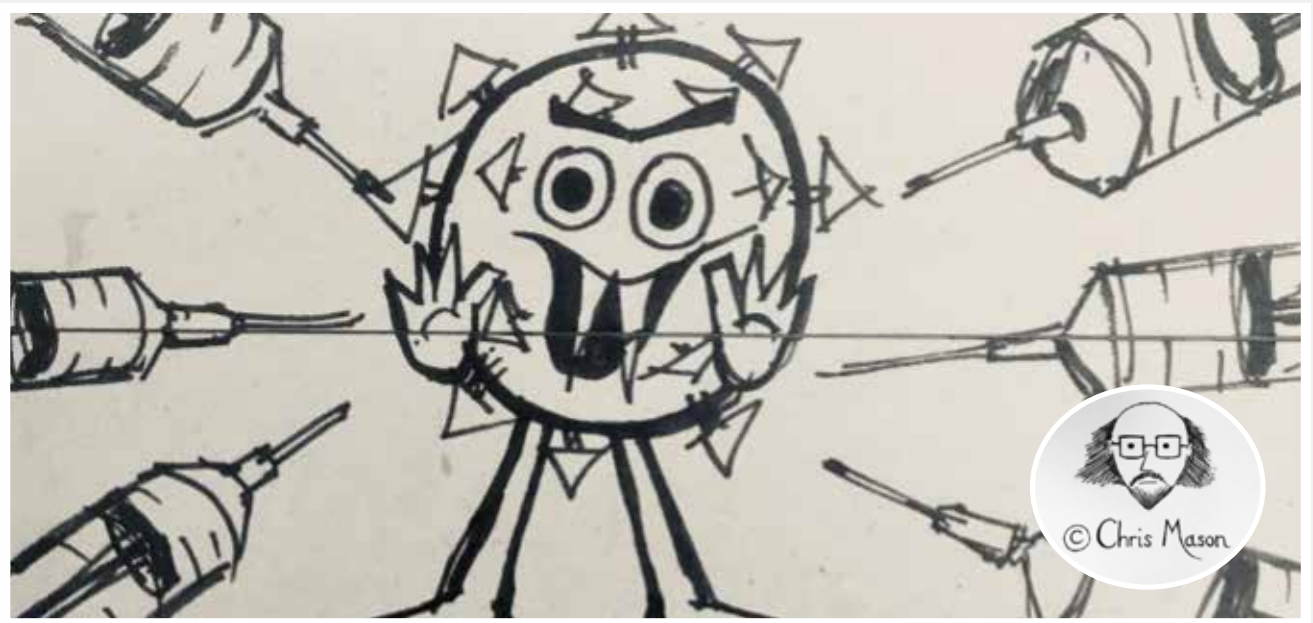
In the early 1990's, working for Lederle, and was invited to set up UK trials of a new vaccine to Haemophilus influenza type b (Hib). The vaccine was based on the then new conjugate technology, which enables or enhances an immune response to the capsular polysaccharide of encapsulated bacteria, such as the Hib, meningococcus (except group b) and the pneumococcus. Soon after, in response to increasing rates of group C meningitis in children, I found myself in the right place when the UK Department of Health called for vaccine companies to work with them to rapidly develop meningococcal group C conjugate vaccines. In late 1999, we were the first company to launch a group C conjugate vaccine, in time to curtail the winter spike of group C meningitis and deaths. In parallel, we were developing the very first pneumococcal conjugate vaccine, a globally important class of vaccine, which has expanded from covering seven serotypes to a point where we are now in clinical trials with a 20-valent pneumococcal conjugate vaccine.

During the subsequent two decades, I was fortunate to work in different companies on vaccines based on various technologies against many infectious diseases, including typhoid, tuberculosis, HPV, infant combination vaccines, Clostridium difficile and many others; some even worked.

Working with vaccines has been immensely satisfying, although paradoxically people soon lose interest in successful vaccines as soon as they reduce cases of the target disease.

> *"...paradoxically people soon lose interest in successful vaccines as soon as they reduce the cases of the target disease..."*

A few years ago, I returned to where I started, in some senses. Lederle Vaccines had become Pfizer vaccines and I am based in Berkshire, close to Oxford. I saw this as coming home to quietly prepare myself for retirement. We were talking with BioNTech about a collaboration to use a new vaccine technology, mRNA, for seasonal influenza vaccines, and I was clinical lead for the program, which looked as though it would take many years. Then SARS-CoV-2 appeared, and I was in the right place to play a key role in the clinical development program for an mRNA COVID vaccine; zero to authorisation for general use in under a year (though much work continues). Retirement on hold. Again, right place, right time to rapidly develop a vaccine for an emerging pathogen using a novel technology. Story of my fortunate and very satisfying career in vaccines.



Memories of Oxford Medicine Part One (1946-66) Dr Derek Hockaday (Age 91)

Dr Derek Hockaday *(1947 Brasenose College), retired consultant physician and endocrinologist*

I'm sorry that this isn't a scholarly and strategic review of the remarkable and unfinished development of the Oxford Medical School since the start of the NHS, but rather scattered memories of my interactions with it, with a heavily personal bias, which is how my mind works these days.

My first experience of Oxford medicine was in 1946 as a schoolboy who had strained a knee playing rugby against a college 2ndXV, so I was taken to A&E at the Radcliffe, and without any imaging they diagnosed correctly that nothing was broken or torn, and that I could walk away with a supportive bandage. A&E was as hectic but much smaller then. A year and a half later, I came up to Brasenose College to read medicine. In the admissions process, I had a viva with Medawar who gave me a cervical vertebra from a manatee for comment - I mumbled something useless, and have always regretted that I didn't say that it was from the neck of a front-row forward. Most of the 1947 matriculants were ex-Service, some from two years in post-war Germany, some who'd been fighting since 1940 and had only just returned from the Far East, but future medics and other scientists and mathematicians were also taken straight from school. This resulted in my humiliation when a notice in the Lodge requested me to collect my bananas from the Bursar as, though turned 18, I still had a child's ration book, which entitled one to a few of the first bananas to land from the West Indies.

The first term was split between Anatomy and Organic Chemistry in the Dyson Perrins Lab; the latter was boring but the lectures in Anatomy, especially from Le Gros Clark on the nervous system, were much better, and relieved the systematic dissection of the formalin-soaked cadavers with accompanying vivas, some from the exquisitely dressed Alice Carleton, with powder-blue rinsed hair and a stinging tongue to reprimand ignorance. In Hilary lectures, practicals and a weekly tutorial in Physiology began alongside anatomy. For my first term, I was farmed out to Keith Taylor, in his lodgings in St Giles', for metabolism and biochemistry, and perhaps because that did come first, I took to it, and found Baldwin's 'Dynamic Aspects of Biochemistry' fascinating with its accounts of Krebs' two cycles. The first, the urea cycle, was to be severely criticised on quantitative grounds by R.B.Fisher in our Schools year, correctly for it did indeed need revision. He later did much work with Dennis Parsons on the perfused gut; Parsons came back from the Far East in my second year with all the new ways of thinking about body fluids and how to describe their contents in mille-moles rather than mille-grams, but initially was so shy that he faced the blackboard and talked to it in a quiet voice: he was the only lecturer for whom I sought a front-row seat, usually much preferring the back row.

George Gordon was the BNC tutor for medics; he seemed a very established figure though only a few years older, but was a splendid tutor, giving a very carefully selected and not overlong reading list each week. In the first two years, working for 1st BM, he taught groups of three or four, and had a system of drawing straws to decide who should read their essay. After I'd drawn the short straw four weeks running, I thought I'd be safe not to write an essay in a 'busy' week. I'd forgotten that chance has no memory, but happily George took my hint of 'Those whom the Gods wish to destroy.....' when I again drew the short one, and moved elsewhere. He occasionally wiled away the minutes while an essay was being read by practising his putting in his large College room, but always knew what had been said.

The whole pre-clinical course took three years and two terms, but George was one of a group of young tutors, who, imbued with the importance of the Honours School of Animal Physiology, thought it should occupy four terms with 'Path and Bac' and Pharmacology, the start of 2nd BM, taken before Schools. As that meant another Trinity term without an exam at the end of it, I gladly climbed on his wagon, but after a year or two the intended reform withered away. After Schools, I decided to stay another year to do a B.Sc in Biochemistry and had a busy but immersive year on the metabolism of pantothenate-deficient rats, whom I remember feeding their special diets on Christmas Day. I saw my supervisor at the beginning and end of the project, but meanwhile had been given much friendly advice and support by Lloyd Stocken, a non-medic and long-standing member of Sir Rudolf Peters' team, which had worked on the British Anti-Lewisite poison gas antidote. Sir Rudolf had a habit of moving his neck highly reminiscent of the bobbing movements of pigeons, on whose hearts he largely worked, and also a liking for effective toxins, such as fluoroacetate, which at that time he thought undetectable, unless one thought to look for fluorine.

It was said that Liddell, the Professor of Physiology, had no sweat glands because he moved so slowly, I suspect for cardiac reasons. The only one of Sherrington's great teams still in Oxford, he lectured at 9am on a Saturday so that his audience would be small, and though his lectures were uninspiring, they were sparingly studded with valuable aphorisms, such as the German version of 'Technique is everything' and 'Movement begins and ends in posture'. The University had recently decided that undergraduates should sign in at lectures they attended, an idea inconceivable in the 1930s, and which we resolutely flouted by attending unsigned.

After clinical studies and first House jobs at the Middlesex Hospital just off London's Oxford Street, I was posted in

1957 for my National Service as a medical officer in the RAMC to Wheatley Military Hospital, I think because Dr Kremer for whom I'd worked in London, along with Ritchie Russell, was one of the Cairo group in British Neurology who'd all served in Egypt during the North African campaign. No history of Oxford medicine is complete without including that unusual centre for Neurology and Neurosurgery for all three of the Armed Forces, for it was the only military hospital regularly visited by NHS consultants, and effectively I was Ritchie's houseman-cum-registrar for almost two years. And we had time to attend rounds at the RI (Radcliffe Infirmary), especially the Thursday afternoon 'Wittery' grand rounds conducted by Leslie Witts, the Nuffield Professor, at which patients from Wheatley were occasionally discussed. One was a lady who'd been investigated in Hong Kong, not least by tapping her lateral ventricles, and who subsequently had bilateral optic atrophy as well as loss of control of her body temperature which she kept around 35 degrees Fahrenheit by obesity and many layers of clothing. Body temperature control was one of the topics of research in George Pickering's multi-facetted laboratory so he was intrigued, and we collaborated on further tests. Allied to the resurfacing of my old biochemical leanings as I sought at Wheatley to investigate by paper chromatography the amino-acids in the CSF which we were regularly tapping, this perhaps underlay a 'phone call I received one June morning from Ian Bush, a distinguished liquid chromatographer working in Pickering's department, to ask if I'd join as a junior lecturer in a project he was starting, to investigate body fluids in patients with psychiatric diseases. By chance I was driving to Cookham near Aldershot that morning to play cricket, and the contrast between the sunny Oxfordshire lanes and the 'Big Smoke' to which I'd vaguely imagined I'd be returning, as well as the paucity of effective treatments for neurological diseases, was enough to make me jump at the chance.

> *"...Pickering was engaged in a desperate battle to save the Clinical School..."*

Pickering's department was on the second floor of a block running north from the central spine of the RI, and perhaps going with his attitude, common then, that research was 'a hobby' and 'fun', housed at least five different interests, from the genesis of fever and body temperature control via phenylketonuria through Ian Bush's group to a major effort by Tony Mitchell and others to understand arteriosclerosis and coronary artery disease. Surprisingly, though Pickering had published a ground-breaking book on Hypertension, there was no one else working on it until the mid-60s when John Ledingham came, with Mike Lee and others, to work on renin. Near the entrance, hung high-up, was a road sign, 'Sir George's Lane', filched from a Hampshire byway; Pickering wasn't one to bow easily, but he was insistent that the sign be taken down and hidden when Enoch Powell, of 'rivers of blood' fame, and then Health Minister, came to visit the RI, perhaps reading Powell's prim and legalistic nature correctly.

Pickering was engaged in a desperate battle to maintain and develop the Clinical School. Nuffield had intended a post-graduate school, such as the Hammersmith became, but the War ensured an out-of-London pre-qualification school. Two years after he came to Oxford from a professorship at St Mary's in London, there's a photo of him sitting with an administrator and that year's student entry of five! His expression is both desperate and resolved, and he succeeded in raising the numbers and its repute through three activities: first, the belief that NHS and University staff should have equal standing, with opportunities for NHS staff to be involved in, or lead, research, and the joint 'A + B' NHS consultancies with two or three university sessions a week out of the total of 11, reserved (theoretically) for research, which had accompanying funding so long as private practice was eschewed: secondly, the realisation that there were many graduating in Cambridge who traditionally, like their Oxford peers, went to London hospitals for clinical training. Backed by Michael Dunnill as Clinical Director, he launched a vigorous campaign in his old university to change that pattern with real success, as reflected in the transformation of Tyngwick from a crude and bawdy review to a talented carefully choreographed musical comedy, however broad. And thirdly, through the changes in staff personnel that time inevitably produced, perhaps especially in 1966 when one Nuffield Chair (Orthopaedics), two consultant surgeons and three consultant physicians were appointed, the last three within three days. It should have been two, but, after Peter Sleight had been appointed to the NHS post linked to cardiology, next day two posts with links to metabolic and endocrine medicine were to be filled from 10 candidates, the interviews starting at 2pm with the aspirants crammed together in a tiny room next to the imposing Board Room. Being a local, and with alphabetical order of interview, I avoided the toxic fumes for an hour and drove out to walk up Forest Hill. I believe the appointments board reduced their possibles to three, two essentially from posts in London hospitals (though John Ledingham was actually then doing his time in America, on renin with Laragh in New York), so Pickering launched a long-drawn-out filibustering discussion interrupted only by one of the three London appointees saying they really must leave to catch their train home. As often happens, it would have been said that any of the three would fill a post competently, and so Pickering assured the Londoners that they could safely leave the actual appointment to a smaller group, just of the Oxford members, which he'd reconvene next morning with their local bias, much to my advantage.

Just two memories of my time as, effectively, Pickering's registrar. One night, I was woken from sleep out at Forest Hill, in our first house, by bright lights and noise. This was a police car, bringing the message that I was wanted at the RI; and they'd come because persistent heavy rain had cut the 'phone line between the Stanton.St.John exchange sub-station and our house. They even offered to drive me in, but my Mini did start, and I thought it easier for the return if I drove myself.

Some in Pickering's department were more academically inclined, some more clinically, and some both. I remember calling a college lodge one evening and asking the porter to go to High Table and tell one of the first category who was dining there, and was also working as a House Physician, to come immediately to the Hospital!

T.D.R.H. 21st April 2021

A Life-Changing Encounter in Oxford: A personal view

Professor Geoffrey Pasvol *(1974 St Catherine's College and Wolfson College), Emeritus Professor of Infection and Tropical Medicine, Imperial College London*

Geoff Pasvol arrived in Oxford from South Africa in June 1974 on a three-year Rhodes Scholarship. A brief, serendipitous proposal by David Weatherall changed not only his intended medical career but the course of his entire life forever. He remained in Oxford for 17 years. In the meantime, Weatherall set about transforming the medical school into what will become the finest on the planet. These two events are unrelated!

In October 1974, I nervously approached the office of David Weatherall (DJW) who had just been appointed Nuffield Professor of Medicine at Oxford. I was in the ramshackle precincts of the old Radcliffe Infirmary on the Woodstock Road; a cold draught blew through the long dim corridors which opened to the exterior by dilapidated, sprung, flexible rubber doors. To me, there was little superficial evidence that I was on the campus of what would become one of the finest medical schools in the world. My intention was to discuss with the professor my plans to study the role of tumour specific antigens in the pathogenesis of adult leukaemia.

Phyllis Woolford, DJW's new secretary, stern but kind, sat by an ancient typewriter. She indicated that the professor was on an important call to Liverpool. Through the half open door, words drifted into the room "Well Herbert, I don't know if I can find anyone footloose and fancy-free in Oxford who might go to the tropics, but I shall have a look around" These words came from a softly spoken individual who, judging by the smell, was smoking a pipe. I cannot deny that I was a little surprised; after all I was on Richard Doll territory! He replaced the receiver and summoned me into the room. I was greeted by a modest, somewhat portly man of medium height, with a Northern accent and seemingly very friendly.

"I am the new DPhil student," I announced. He smiled and replied, "Would you like to go to The Gambia?" I was dumbfounded; I had arrived at the beginning of June by sea on the sleek lavender hulled Pendennis Castle of the Union Castle Shipping Line from Cape Town to indulge in the magic of university life in Oxford and now this suggestion! Besides which, I hadn't a clue where The Gambia was! To avoid embarrassment I tactfully replied, "When do I leave Sir?" "In six or so weeks as soon as we have sorted out your visa. We have made an initial finding on a few malarial blood films from East Africa that looks interesting and needs corroboration. It will only be for a few weeks and then you can embark on your leukaemia research". I scurried back to college (St Cats) to consult my concise Phillips Concorde World Atlas.

At the MRC Unit in The Gambia, I met a certain bright-eyed Scotsman, Iain Wilson, who showed me how to grow malarial parasites in vitro and we almost succeeded in doing this continuously for the first time but for being pipped at the post. I was hooked on tropical medicine, never to return to haematology or genetics as a clinical specialty. Back in Oxford, a magical period of research ensued, interspersed by five short trips to Africa (conveniently November to February!). We were a small band of research workers in DJW's lab and there was never a dearth of technical or laboratory help coming from John Clegg (Professor's close co-worker), Bill Wood or Doug Higgs (a future head of the Institute of Molecular Medicine and lifelong friend) or others. I spent much of my time in the dark (room) scrutinising malarial slides prepared abroad and brought back to Oxford. The work raced ahead and within five years our research had produced three papers in *Nature* and one in *The Lancet* - a lucky stroke indeed! We were studying one of the best examples of Darwinian natural selection in man, i.e. malaria and the cellular mechanism by which the haemoglobin variants, especially thalassaemia might protect against malaria.

> *"...This student will go far" said David Weatherall of John Bell after John's first case presentation on the NDM...*

Tropical Medicine (Geographic Medicine, Global Medicine - call it what you will) was given a tremendous boost when David Warrell and Nick White ventured to Thailand in 1979 to study the pathogenesis of severe malaria. DJW had been in discussion with Peter Williams, the then director of the Wellcome Trust who was at the time operating from a relatively small set of rooms at 1 Park Square West on the Euston Road; very much like a family business. With the Trust's support the future of the Oxford Tropical Clinical Centre was assured and the rest as they say is history.

Back in Oxford, the slightly dishevelled but alarmingly clever Tim Peto and I were heading out on training in General Medicine and Infectious Diseases (ID), the latter under the formidable control of Bent Juel Jensen (JJ), Medical Officer to the University. DJW and JJ could not have been more contrasting, the one cool, calm, and measured, the other fiery, excitable, and irascible but both always kind and loyal to us (Fig.1). The ID ward (John Warin) was at the Slade hospital in Headington, near the ring road - at the time truly isolated!

Figure 1: *Research and clinical mentors David Weatherall (DJW) and Bent Juel Jensen (JJ) on an NDM party invitation (artist unidentified).*

However, for General Medicine there was John Ledingham, a most inspirational and respected clinician and teacher. He had the canniest sense of expression and I recall one with descriptive references to a COPD patient as "puffing like a landed salmon"! The highlight of the firm was the weekly NDM clinical case presentation which would take place on a Thursday morning in a quaint little seminar room in the infirmary lined on either side with red plastic-covered chairs against each wall facing inwards. A strongly accented Canadian medical student in 1975 presented a case using the 'epidiascope' (overhead projector) of shingles treated with adenosine arabinoside, a new drug masterminded by the Nobel laureate Gertrude B Elion. He did this without hesitation, digression or circumlocution. His deep, compelling, authoritative words resonated around the assembled throng. It was the voice of John Bell. "This student will go far, '' said DJW. It was the start of John Bell's illustrious career in Oxford, and I was there! He would become Nuffield Professor of Medicine in 1989, Regius Professor in 1992 and go on to shape what DJW had started, into an operation of international repute.

On my third visit to The Gambia in 1977, perhaps the most important event in my life occurred. It was at a Guy Fawkes party at one of the doctor's houses in the MRC compound and there were fireworks indeed when I met my future wife, Kate France, a VSO (Volunteer Service Overseas) architect.

Figure 2: *Pasvol receiving inspirational clinical research advice in 1989 from Nick White in characteristic pose on the River Kwai.*

Under mother-in-law's orders, we were married within six months; and 44 years later we are both present to tell the tale. So much for life changing encounters.

A substantial material advance occurred in 1980 when the hospital transferred to a new building on the John Radcliffe site. Gone were the draughty corridors of old and in came a swanky hospital with purpose-built research laboratories. It was in 1985, in my lab on the fifth floor, that I was joined by a classy triumvirate of Andrew McMichael, Alain Townsend and Francis Gotch! I was in good scientific company to say the least. A second major move was to the Institute of Medical Molecular Medicine in 1989. Peter Radcliffe moved into my old laboratory and I would like to think that perhaps the inklings of his research to become a Nobel Laureate were initiated in my former workspace. I was now a Wellcome Senior Fellow.

> *"...Oxford voted in 2021 as the number one medical school in the world for 8 consecutive years...*

I have often reflected on my time at Oxford. Over the 17 years, I had the privilege of being the Deputy University Medical Officer vaccinating all orders of employees on their worldwide travels (JJ was particularly keen on the exotic, for example, rabies, plague, Rocky Mountain Spotted Fever, and others!). I had been clinical organiser of the final MB exam

Figure 3a: *How to build a paediatric ITU in three months in Kilifi Kenya, 1990 (before)*

Figure 3b: *How to build a paediatric ITU in three months in Kilifi Kenya, 1990 (after)*

for three years, acting medical tutor for two years and had exposure to hundreds of medical students, many of whom have subsequently carved their names illustriously in so many capacities on the national and international front. My role as firstly member, then vice chairman and ultimately, chairman of the Central Oxford Research Ethics Committee, led me to be acquainted with wonderful movers and shakers amongst the organisation's researchers. But an underlying brooding possessed me - I had not looked after patients in a major way.

At this point (1988), David Warrell invited me to be the new scientific leader of the KEMRI Oxford Medical unit which was about to be launched in Kilifi, a research site on the coast of Kenya. As much as I had enjoyed the lab and research for nearly 15 years, I felt in need of a change in perspective. After all, I had studied medicine to look after patients. I visited the agile, unstoppable, and enthusiastic Nick White in Thailand for clinical research inspiration (Fig.2) and off I went once again to Africa. Our priority was to build a paediatric intensive care unit which we duly did in under three months! (Fig.3)

In Kilifi, my dilemma was compounded by a letter from DJW. "I would like to put you up for the Wellcome's new permanent senior lectureship scheme". I temporarily hesitated but when a chair at St Mary's Paddington London arose, I applied and returned to the UK for three days for a successful interview.

Although I was leaving a family and a father figure, I was joining another flourishing institution shortly to become an integral part of Imperial College London. It was not without deep sorrow that I cut the apron strings. It was therefore reassuring when I received a letter from DJW saying how much he had appreciated having me on the NDM. "It was great to think that the cheeky South African who wandered into my office during the first week (of his time in Oxford) is now a professor, but more seriously you've given a great deal to the department and I appreciate it enormously...". What more could I expect! As an accolade coming from DJW, it provided much solace.

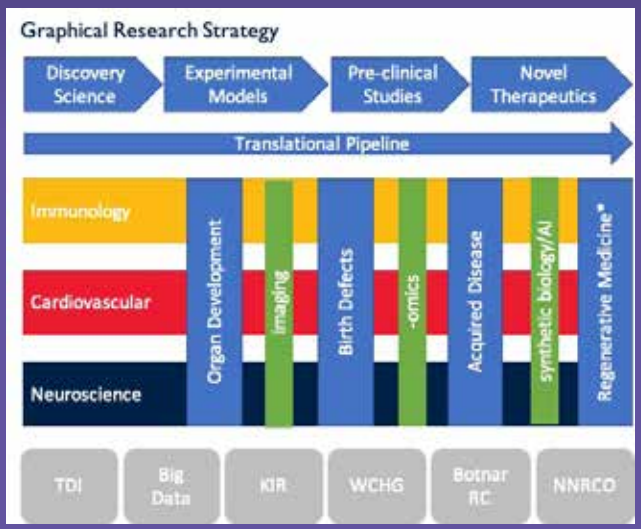
The story of the rise of Oxford Medical School, when it is ultimately told in detail, will surely highlight David Weatherall as one of the first catalysts to move the department into the 'molecular' or '-omics' age (genomics, proteomics and metabolomics"). The meteoric John Bell introduced a capacity for big data, technological advances and entrepreneurial input from industry and endowments that led on to a 'golden age' in which the medical school was voted for eight consecutive years (2014 to 2021) by *The Times* Higher Education Supplement as the best medical school in the world. I would like to think that each and every one of us alumni of Oxford have made a contribution, however small, to this final achievement of a world beating medical school of which we can all be proud.

Institute of Developmental & Regenerative Medicine

Professor Paul Riley *(British Heart Foundation Professor of Regenerative Medicine, IDRM Director) and* ***Professor Georg Holländer*** *(Hoffmann and Action Medical Research Professor of Developmental Medicine)*

The Institute of Developmental and Regenerative Medicine is poised to make exciting new discoveries in how to restore or replace lost tissues in the heart, brain and immune system. There is now a very real possibility of developing new drugs and therapeutic strategies to treat birth defects or tissue injury arising from adult disease. For example, using drugs to reactivate foetal reprogramming following a heart attack, targeting nucleic acid delivery to treat Duchenne muscular dystrophy and using gene therapy to stimulate a deficient immune system.

Two thirds of all deaths world-wide are due to non-communicable diseases; many of these are cardiovascular, neurological or immune system disorders that have a developmental origin and represent an urgent unmet clinical need. To make an impact in this space and to facilitate the discovery of new regenerative therapies the Medical Sciences Division at Oxford, has established the Institute of Developmental and Regenerative Medicine (IDRM), a bold new strategic initiative which will transform the local, national and international landscape in regenerative



medicine. At its core, the IDRM is a formal merger of developmental biology and regenerative medicine with a focus on understanding how tissues and organs are formed during normal development to inform on strategies to repair and regenerate the same tissues and organs when injured or diseased. The Institute will bring together 15-20 world-leading research groups, comprising 240 cardiovascular, neuroscience and immunology scientists integrating their expertise, combining experimental and computational biology with advanced bioimaging, multiple "-omics" platforms, machine learning, artificial intelligence and mathematical modelling; working with University colleagues in Big Data, Target Discovery, Maths and Biomedical Engineering and with clinicians at the John Radcliffe and Churchill Hospitals in Oxford.

> "*...Regenerative Medicine is defined as "the process of replacing or regenerating human cells, tissues or organs to restore or establish normal function"* [Sydney Brenner (1927-2019); 2002 Nobel Laureate and Alumnus of Exeter College, Oxford]...

There have been few clinical success stories in regenerative medicine to-date. Stem cell therapy is the most widely explored but remains very challenging. With the notable exception of the use of hematopoietic stem cells in autologous and allogeneic transplantation for blood and some metabolic and immunological disorders, it remains unclear which is the best source of cells for transplantation. Most donor cells do not survive in what is a hostile pro-inflammatory environment with ensuing tissue scarring and fibrosis. At best, there has been modest and transient clinical benefit; most notably in the cardiovascular setting, where cell-therapy trials to treat patients following acute myocardial infarction have largely failed to deliver on the pre-clinical promise. The other major issue is that these trials have not stratified the patients for important risk factors and prognostic indicators, such as age, sex, ancestry, and pre-existing co-morbidities. The end-result being compromised efficacy. It is becoming increasingly apparent that stratifying patients, alongside the use of improved biomarkers to predict outcome, are pre-requisites for a successful trial design. That said, there have been some notable stem cell applications, in a limited number of patients, including the treatment of spinal cord injury and corneal damage.

Significant clinical potential exists in other areas of regenerative medicine, such as gene replacement therapy and gene editing, currently being applied, for example, to induce "exon-skipping" as a potential treatment for Duchenne muscular dystrophy. Tissue engineering represents another promising approach; utilising smart materials to facilitate cell delivery and survival, or via the generation of patches for tissue repair. 3D bioprinting of organs is also being actively explored, with the goal to deliver an unlimited supply of replacement "parts". These platforms are either at a preclinical stage, or part of ongoing trials, and have yet to be translated to treat a vast array of diseases and injuries that can potentially be cured by regenerative medicine. These include Alzheimer's, COPD, type 1 diabetes, kidney disease, multiple sclerosis, muscular dystrophy, myocardial infarction/heart failure, osteoarthritis, Parkinson's disease, rheumatoid arthritis, systemic lupus erythematosus and sports injuries. Hence, there is an urgent unmet clinical need for new drugs and treatments to tackle some of these debilitating conditions.

The IDRM's IMS-Tetsuya Nakamura Building is currently under construction; the "topping-out" ceremony was 15th December 2021 and the Institute will open its doors in January 2022.

Please visit **www.idrm.ox.ac.uk** for further details.

Professor Paul Riley, Professor Georg Holländer and Professor Matthew Wood (Professor of Neuroscience)

Twin Tales: Paediatric Surgery

Dr Dan Carroll *(1989 Magdalen College), Associate Professor in Paediatric Surgery, James Cook University, Australia*

"..Did you exchange a walk-on part in the war, For a leading role in a cage. How I wish, I wish you were here.."
- Pink Floyd.

It was only a few weeks ago that I was asked if I could contribute something for *Oxford Medicine*, and it has given me a chance to reflect on the difficult times we find ourselves in. I had a wonderful and formative time at Oxford where many of you may remember me, not for any outstanding personal contribution, but because I was one half of a pair of identical twins studying medicine. My career has taken me far away from the safe and familiar NHS (consultant paediatric urologist in Cambridge). Nine years ago, I washed up in Tropical North Queensland as a paediatric surgeon to a massive geographical area. For those of you unfamiliar with the geography of North Queensland, we cover an area roughly the size of the UK/France and Germany combined but with a population of around one million. It was a big step to leave family and friends (and most particularly my brother) far away. It was a huge decision for us as a family, and I am lucky to have the support of my wife (Dr Charlotte Slaney, 1992 LMH) who is working as a radiologist here in Townsville.

My working life here in Australia is both familiar and different to life in the UK. Patients remain the same, and, as for most of us are central to my enthusiasm for the job, our clinical knowledge and skills remain a transferable currency.

Torres Strait Islanders (ATSI) and aboriginal peoples make up around 40 per cent of my patient group and working with them was a strong motivating factor in my move to Tropical North Queensland. They suffer from systemic disadvantage throughout their lives. The inequalities start emerging from foetal life and continue throughout childhood into their adult lives. The huge variety of challenges from the many diverse groups provides perhaps my most rewarding and inspiring day-to-day work. The community elders and our wonderful Indigenous Health Liaison officers at the hospital are enormously helpful in connecting with the families of sick and injured children and building bridges with these communities. I have been privileged to work with many nurses and doctors from indigenous backgrounds as well as helping to train medical students from indigenous backgrounds at James Cook University medical school. I continue to look at outcomes and conduct research into improving outcomes in ATSI children with burns.

Paediatric surgery is an exciting field at the moment. Of particular importance are the **improvements in antenatal diagnosis leading** to new frontiers of treatment opening up for our patients with the **potential for fetal surgery**, antenatal interventions and perhaps most importantly a clearer understanding of the natural history of paediatric surgical conditions. In addition, paediatric surgeons find themselves in the forefront of developing **minimally invasive surgery** even for our smallest patients, with even technically challenging operations such as oesophageal atresia and pyeloplasties now being performed using 'keyhole' surgery. The challenge to develop new instruments and imaging to assist surgery has been met by many paediatric surgeons combining with medical device companies to allow surgeries that would have been considered impossible at the start of my training. As I have an interest in paediatric burns surgery, the new frontiers and understanding we have in dealing with scars and **remodelling of burns scars using lasers to 'sculpt' and remodel difficult scars** is something I am working on at the moment in our paediatric burns patients.

Despite the advantages, the call of home is still strong for most of us ex-pats, and the inability to travel and see friends and family is a big worry. All of a sudden the world is larger than it ever was, and I am sure that I am not alone in my feelings of homesickness. Thank goodness for the telecommunications of the 21st century that let us stay in touch with friends and family. Whilst we have so far escaped the worst of the global pandemic, our thoughts are often taken back to home and our friends and colleagues in the UK who we can no longer visit. I hope that all my friends reading this are well, and from afar it would seem that the UK is heading out of the other side of this faster than us here in Australia.

For those of you considering a sea-change after what must have been a harrowing year, please consider Australia, particularly thinking outside of the box of the big cities. Regional and rural Australia is an exciting and interesting place to live and work, although the workload can be very hard particularly in disciplines with small on-call rosters. Wishing you and your families all the best from the sunny tropics.

Clinical School intake photograph, 1992

Twin Tales: Paediatric Medicine

Dr Will Carroll *(1989 The Queen's College), Consultant Paediatrician; Honorary Reader in Child Health; RCPH Officer for Research; Deputy Clinical Tutor; Editor-in-Chief Paediatrics and Child Health and NIHR - Clinical Research Scholar, Staffordshire Children's Hospital at Royal Stoke; University Hospitals of the North Midlands, Keele University*

So, depending upon your perspective, this is the view from the 'right side' of the world and possibly the right half of paediatrics. In 1994, I decided that children were infinitely more entertaining than adults. Not being particularly attracted to the world of general practice at the time, I decided that I would set out to become a paediatrician. I can honestly say that I have never regretted the choice for a moment.

I seem to recall that I made my twin promise that he would not pursue a career in paediatrics. I personally have always suspected that he decided to pursue paediatric surgery just to annoy me. I was asked to write a short update on what is new in UK Paediatrics to complement a short piece from my twin.

The year 2020 (and the first part of 2021), have been a very different year for all of us. I had hoped to see Dan at least once this year (if not twice) but 'the virus that has come to dominate our lives' has put pay to all of that. We have seen some remarkable changes in paediatrics over the year. Not all of them are COVID-19 related.

As a respiratory paediatrician, it has been enormously gratifying to see the amazing effects of the new treatments for a range of previously fatal diseases. The newer cystic fibrosis transmembrane regulators (CFTR) were anxiously awaited for the last two to three years. The research had indicated that the new 'triple therapy', Kaftrio, would have dramatic effects. I can confirm that these are real and substantial. I have seen children and young people's lives transformed by these new treatments in a way that I hardly dared hope for. Indeed, the effects are so dramatic that many cystic fibrosis teams are seriously wondering whether they will need to 'downsize'. For now, I am left wondering how quickly we can begin to reduce some of the other treatments required.

The reaction of one of my patients to the news that **Kaftrio was funded in the UK in November 2019** was priceless. Indeed, her authentic reaction still makes me cry. If you want to see what it means to many of the families please do follow the story at: **www.uhdb.nhs.uk/latest-news/nurse-beth-invited-to-number-10-after-daughters-reaction-goes-viral-6207.** It also might explain why at 50 years old I still look forward to a day in clinic.

A second area where there has been **significant change is in the treatment of spinal muscular atrophy (SMA**). Whilst the textbooks still describe cystic fibrosis as the 'commonest inherited, life-shortening condition affecting white children', spinal muscular atrophy type 1 is the commonest genetic condition resulting in infant death. I must admit to paying it less attention in medical school. However, it has been my privilege to care for dozens of children with different types of SMA over the past 20 years. For these children, the shifts in the clinical landscape have been no less seismic in the last one to two years.

> *"...it has been enormously gratifying to see the amazing effects of the new treatments for a range of previously fatal diseases...*

For those who like a bit of science (and I am sure that is most of you), then a useful explanation of SMA (an exon-skipping disease) and how some of the new treatments might help is found at: **smauk.org.uk/more-detail-on-how-nusinersen-works-in-sma**

I have been lucky enough to work in a centre (Stoke-on-Trent) that has been delivering Nusinersin, a new intrathecal treatment to children with SMA1. Its effects are impressive, but look set to be eclipsed by the arrival of gene therapy in the form of Zolgensma. In fact, I write on the day when the Evelina Children's Hospital in London has delivered the first dose of this treatment 'on the NHS'. **www.bbc.co.uk/news/uk-57309613**

I live in hope that Stoke-on-Trent will be added to the list of centres approved to deliver this life-changing treatment soon.

I am sure that other paediatricians would have been able to bring other examples of dramatic changes in the last year. If I missed your favourite advance, then please accept my apologies. Nonetheless, it remains clear that we really are living in 'exciting times' and not always for the wrong reasons.

I pray that 2022 sees an end to the pandemic and a return to travel, especially for those who are separated from their families. I hear reassuring news from our friends and colleagues on SAGE that some type of 'normal' might return next year. Let's hope that these wise folk, many Oxford alumni, live up to their name.

Engineering Innovations

Professor Lionel Tarassenko
CBE FREng FMedSci (1975 Keble College), Professor of Electrical Engineering, Institute of Biomedical Engineering, Department of Engineering Science; President, Reuben College, University of Oxford, and Founder-Director Oxehealth, R&D Director Sensyne Health

Since March 2020, the focus of the Biomedical Signal Processing & Machine Learning (BSP-ML) research group has been on adapting the technology, apps and machine learning we developed in the last decade for the fight against COVID-19. This has been achieved through remote patient monitoring, better patient stratification and improved diagnostics. Some of the work has been done in collaboration with Sensyne Health and Oxehealth (two companies on the Oxford Science Park). Here we describe four of the key projects in which our research group, based at the Institute of Biomedical Engineering, has been involved.

Self-monitoring of blood pressure during pregnancy (BPm-Health)

BPm-Health is a blood pressure management system which helps expectant mothers to self-monitor their blood pressure, communicating their results to their healthcare team remotely rather than during face-to-face clinic appointments. It has been used during the pandemic to monitor pregnant women at risk of developing hypertension and progressing to pre-eclampsia. Automated feedback from the app and remote calls with clinicians has kept these at-risk women away from hospital during the COVID-19 pandemic, to minimise the risk of infection.

Women are sent reminders when it is time to take a blood pressure reading and they can then record data on the patient app. The app displays advice on what women should do, dependent on the results submitted. The formal launch of the BPm-Health product came after the successful recruitment of a 3,000-participant multicentre trial (BuMP) involving 15 NHS Trusts (Dougall et al., 2020). The system which we had developed in the IBME was transferred to Sensyne Health in record time. It was approved by the Royal College of Obstetricians and Gynaecologists and went live nationally in May 2020 (see **www.sensynehealth.com/bpm-health**).

Video camera technology for remote triage of suspected COVID-19 patients

For the last decade, we have been developing software algorithms to monitor breathing rate and heart rate using a video camera (including the webcam in a smartphone), and these algorithms were previously licensed to Oxehealth (**www.oxehealth.com**). The company's main product is now a system which uses a video camera and infrared illumination in a secure housing to enable clinicians to take breathing and heart rate observations remotely from patients in their rooms. The product is a CE-marked Class II(a) and FDA-approved (a world first) medical device: no device is attached to the patient, reducing infection risk, and staff take observations from a separate location, minimising contact with patients. The system has been deployed in hundreds of rooms in 30 per cent of mental health NHS Trusts in England (Lloyd-Jukes et al., 2021). It was used to monitor patients with suspected COVID-19 symptoms in those Trusts, and by GPs in Oxfordshire to screen patients in a dedicated "COVID-19 hub" in East Oxford.

Monitoring of isolated in-hospital patients using wearables

In the early stages of the pandemic, there was a fear that the lack of knowledge about the dynamics of virus transmission and initial shortages of personal protective equipment could lead to an increased spread of infection in hospital clinical staff. Continuous vital-sign monitoring enables the identification of the rapid desaturation caused by the SARS-CoV-2 virus, and intervention with corrective treatment at the earliest opportunity (for example, via additional oxygen therapy). However, vital-sign monitoring tools used in isolation wards (bedside monitors), were not ideal for active, ambulatory COVID-19 patients. Furthermore, point-of-care devices require staff to be present in the patient isolation rooms to take accurate vital-sign measurements, increasing the risk of spreading the infection.

At the end of February 2020, it became clear that the technology and software that we had been developing for monitoring high-risk ambulatory patients (the "Virtual High-Dependency Unit") could be adapted for the isolation ward for COVID-19 patients in the John Radcliffe Hospital in Oxford. For those COVID-19 patients with no clinical requirement to be managed on a ventilator, or stepping down from intensive care, it is important for their recovery that they should continue to remain ambulatory, and so the wearable technology is ideal. Our research group worked tirelessly throughout the first three weeks of March 2020 to ensure that the modified wearable monitoring system (a wrist-worn pulse oximeter and chest patch for heart rate, breathing rate and temperature, with Bluetooth connection to an

Android tablet at the bedside) could be deployed soon after the opening of the isolation ward. The system went live with its first four ambulatory patients on the John Warin Ward on Monday 23 March 2020, the day that the first national lockdown started.

The wearables system uses web-based architecture and protocols (HTTP and WebSockets) to transmit the vital-sign data in real time from the Bluetooth Low-Energy (BLE) and Wi-Fi enabled Android tablet devices, operating as patient data collection devices by the bedside in the isolation rooms, into a clinician dashboard interface available remotely via any modern web-browser. Fault-tolerant software strategies are used to reconnect the wearables automatically, during intermittent BLE disconnections, avoiding the need for nurses to enter the isolation ward to reset the patient monitoring equipment.

The remote dashboard also displays the vital-sign observations made by the nurses and entered by a separate system into the hospital electronic Track & Trigger record (eT&T). The latter is displayed alongside the continuous wearable data, allowing nurses to review both sources of vital-sign data in one consistent augmented e-T&T screen, and to track the physiological status of the patients in real-time.

System usage has been found to follow the two main COVID-19 wave trends, with half of the patients on the isolation ward monitored during the peak of hospital admissions in both of the main waves (April to July 2020 and December 2020 to March 2021). During the first wave, patients were monitored for a median of 31.5 [8.8, 75.4] hours, representing 88.1 [62.5, 94.5] per cent of the median time they were registered in the system. By the end of the second wave (late March 2021), 167 patients had been monitored for an overall 320 patient-days.

Understanding the trajectory of the COVID-19 disease

We analysed the Electronic Patient Record (EPR) data of 497 adult patients with COVID-19 admitted to the John Radcliffe Hospital from early March to late April 2020, and compared it with the EPR data from a cohort of patients admitted to the same hospital between 2013 and 2017 with viral pneumonia (the closest equivalent).

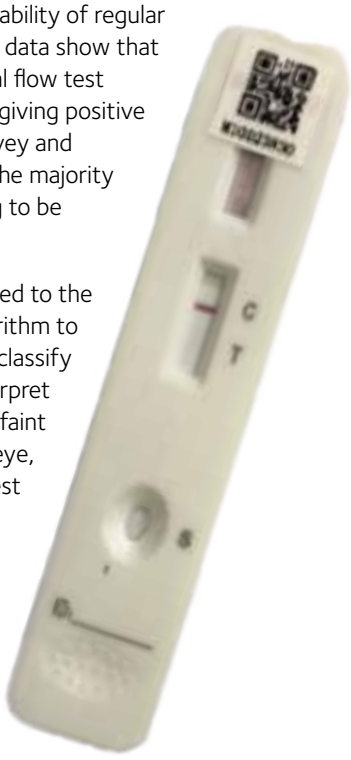
Our analysis showed that patients with COVID-19 who deteriorate in hospital experience rapidly-worsening respiratory failure (with low oxygen saturations even on high inspired oxygen), but with only minor abnormalities in other vital signs. This deterioration is much more rapid than for patients with viral pneumonia. As a result, we proposed a new early warning score for COVID-19 patients (Pimentel et al., 2020).

App for lateral flow tests

The CVm-Health (FACTS) app was designed to enable Oxford University staff and students enrolled in the FACTS clinical study (Chief Investigator: Professor Richard Hobbs FMedSci, Head of the Nuffield Department of Primary Health Care Sciences) to use Innova Lateral Flow Tests (LFTs) and, after each test, use the app to record their test result by taking a time-stamped photo using their smartphone's camera. The data was then uploaded by the app to a secure Sensyne Health database in the Microsoft Azure cloud, with a "dashboard" giving a list of those who self-tested that day, as well as their test result (positive, negative or inconclusive) automatically generated.

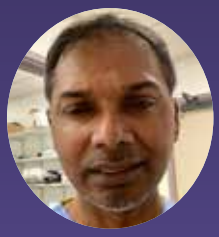
The app and FACTS study went live in Merton and St Hilda's colleges at the beginning of November 2020, and continued until mid-January 2021. There were 825 participants in the study in mid-December. The number of positive tests was remarkably low, of the order of 0.2 per cent of participants.

A paper describing the results of the FACTS study has been written and submitted for publication (Hirst et al., 2021). It concludes that the study provided the first evidence on recruitment, retention and acceptability of regular COVID-19 self-testing. Quantitative data show that acceptability of completing the lateral flow test swab was positive, with 91 per cent giving positive feedback via the phone app. The survey and qualitative interviews revealed that the majority of participants found the self-testing to be acceptable and valued.



Further work at Sensyne Health has led to the development of a deep learning algorithm to analyse the photo and automatically classify the test. The algorithm is able to interpret difficult-to-read lines, including very faint lines, often not visible to the human eye, thereby improving the accuracy of test reading (**www.sensynehealth.com/magnifeye**).

Innovations in Managing Coronary Disease: Looking forward to the future



Dr Steve Ramcharitar *(1993 St Edmund Hall), Interventional Cardiologist at the Great Western Hospital, Swindon*

Heart disease is the number one cause of death globally with four out of five cardiovascular deaths due to heart attacks or stroke. Epidemiologists have played a vital role in determining the risk factors, such as raised blood pressure, glucose, lipids and obesity, but heart attacks still cause more than 73,000 deaths in the UK each year with around two million people affected by angina. The enormity of the problems results in continuous innovations to try and understand the pathogenesis and with this comes novel tools to diagnose and treat coronary disease.

The field of interventional cardiology and vascular radiology started with Werner Forssmann (Noble Prize 1957) who took a radiograph of his own coronary arteries by self-catheterisation of his heart through his arm. However, it took almost a century to address the limitation of two dimensional X-ray imaging, overlapping coronary arteries, disparities in vessel sizing through foreshortening in certain angiographic views, prolonged procedures, increased contrast agent usage, and the associated risks. **Computer Tomography Coronary Angiography (CTCA)** addresses these problems to provide a three-dimensional image of the coronary artery tree, allowing rotation and manipulation of the image to find the best views to perform an intervention such as placing a stent – a metal conduit that is used to keep an otherwise narrowed arteriosclerotic vessel patent to restore blood flow and treat angina.
Arteriosclerotic plaques within the arterial vessel wall can be directly visualised using the high resolution modern CTCA machines. Thus the entire disease can be accurately mapped and the type of plaques determined, for example, calcified, fibrous or lipid rich that may make it prone to rupture - so called 'vulnerability'. The bigger the plaque burden, the higher the risk of complete vessel occlusion causing significant heart attacks. Having all this information beforehand certainly is beneficial to procedural planning and intervention. But not all vessels may need treatment. Indeed, there is much debate on whether placing a stent in a coronary artery offers a mortality or prognostic advantage or if it is merely for symptomatic relief. In fact, studies have shown that medical treatment may be as good as intervention in particular patient subsets.

So what determines the need to treat an artery? Location and severity of narrowing. Disease high up (proximal) in the coronary tree causes a large amount of damage if the vessel becomes occluded; the interventionist relies on physiology to guide stenting. The severity of narrowing is determined by a ratio of the flow before and after it using a guidewire with pressure sensor at its tip and adenosine to increase flow in the vascular bed. Innovations in software means the pressure change can now be done without adenosine by comparing fixed points during the cardiac cycle so called resting indices. When the pressure decreases by a certain amount, the vessel is deemed flow limiting and may allow stenting to proceed. Invasive physiologic testing carries potential risks such as vessel trauma, wire failure and patient intolerance. Patients who may not have physiologically significant narrowing will be subjected to these risks. Here again CTCA has an advantage. By transferring electronically via the Cloud the CTCA dataset, a US company HeartFlow® can determine flow dynamics of the narrowing non-invasively with the results sent to the referring hospital within hours. HeartFlow® utilises computational flow dynamics with advanced mathematical algorithms to account for myocardial resistance, pressure, velocity, density and temperature in a moving fluid and predict changes over a coronary narrowing during hyperaemia without needing an invasive vasodilator drug. A form of artificial intelligence known as deep learning is used to optimise and enhance performance continually. This technology has changed the diagnostic potential of patients presenting with chest pains particularly in low risk patients. NICE is still evaluating its cost effectiveness against standard care where traditional non-invasive tests might be used.

Other technologies are available to create three dimensional images of the coronary tree from the traditional two dimensional angiography with some allowing the use of software to mimic virtual stenting. Unlike CTCA utilising Heartflow, a prior invasive procedure is needed to get the angiographic pictures first so that three dimensional images can be constructed from two orthogonal planes. But the beauty of using three dimensional imaging, either through reconstruction or CTCA, means that they can be co-registered with live imaging at a later stage in order to perform an interventional procedure and thus may limit procedural time, contrast and radiation. It may also offer **a way to Robotic Percutaneous Coronary Intervention (PCI)** in the future. At present, the latter remains an interventional toy rather than a tool.

Sometimes looking inside the artery itself offers useful information on the pathologic processes. In coronary intervention, two main tools are used, one relies on **intravascular ultrasound (IVUS)** and the other uses light – **optical coherence tomography (OCT)**. Both are able to give information about plaque structure with OCT. They particularly give incredible details on the stent apposition to the vessel wall and the mechanism of stent failure. Today, both technologies offer co-registration to the live angiographic image for more accurate procedures.

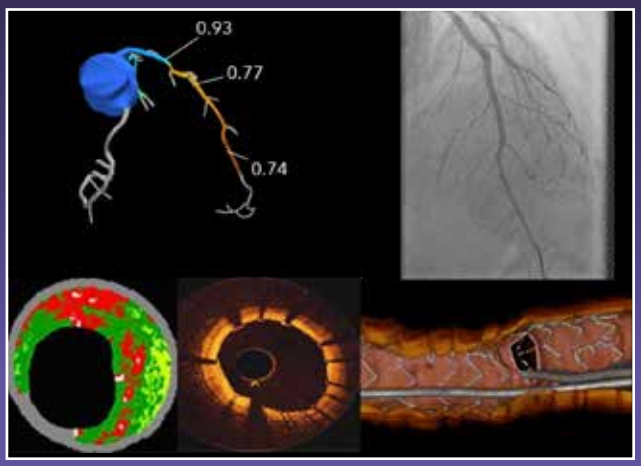


Figure 1: *60yo male, having had a CTCA with Heartflow analysis, demonstrating significant flow limitation in left anterior decendens (<0.80 significant). Subsequent invasive angiography corroborated findings with virtual histology IVUS showing fibro-fatty high burden lipid rich plaque. OCT showed excellent stent apposition with 3D OCT chowing preservation of the ostium of the diagonal side branch after stent deployment.*

In combinations, they can assess plaque vulnerability but at present we do not know if shielding a vulnerable plaque with a stent is advantageous. Much work is needed to try and understand what makes a plaque rupture. What we do know is that inflammation is probably the main driver, hence why it is important that hypercholesterolemia, smoking, diabetes and hypertension are addressed.

Of these all these risk factors, the emergence of new technology to manage hypertension is being evaluated by interventional cardiologists. By inserting a **radiofrequency (RF) multi-electrode ablation catheter** in the main renal artery, discrete amounts of energy can be delivered to burn the afferent nerves that control blood pressure. Early studies on the technology have had a mixed picture but recent trials have shown a degree of optimism, lowering blood pressure by on average by 14mmHg. There is no data to suggest that it can eliminate the need for pharmacology but it is an exciting new field.

Interventional cardiology is driven by innovation and the ability for cardiologists to embrace novel technology in the treatment of complex patients. The close working partnerships with the industry will continue to be a driver, creating opportunities for research in both secondary and tertiary centres. I have touched on a few aspects of coronary interventions which I utilise in my own practice but there are interventional cardiologists working in the ever growing area of structural intervention – involving percutaneous trans-aortic valve insertion (TAVI), closure of patent foramen ovale and stapling leaky valves with specialised clips to fix their regurgitant flow. It's an exciting time to be involved in interventional cardiology. With so much new technology I still feel as excited as a medical student.

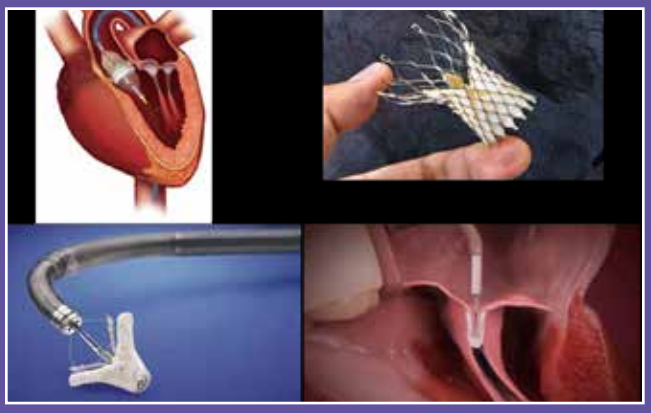


Figure 2: *Trans aortic valve implantation and mitral clips are now being routinely used, especially in surgical turn down patients – but this may become the default as the technology and procedure improves. During COVID-19, because of the early patient mobilisation and not requiring ITU stays, these procedures became a life saver for a large number of very ill patients with heart failure and other symptoms related to narrow or leaky heart valves. In some centres, they were performed as a day case which is now the norm with coronary intervention.*

Optimism from the Frontlines

Dr William Seligman
(2000 Magdalen College), Specialist Registrar in Anaesthetics and Intensive Care Medicine, London

It was with relief, delight, and of course humility that the doors of our 'surge ICU' (read surgical ward converted into a makeshift ICU) in a Central London hospital closed for the last time at the end of March 2021, signalling the end of what was quite frankly a brutal winter.

While we were blessed this time around with treatments that have been proven to reduce the risk of severe illness and death, and with the vaccines representing the light at the end of the tunnel shining ever more brightly, nevertheless, this wave appeared to impact younger, healthier patients than one year ago. Quite why this was, we don't fully understand. Was it because of the new variants? Was it because many of our most vulnerable had been vaccinated, were either still shielding or had sadly already died from the disease?

In any case, with the vaccine rollout proceeding at pace, I am enormously hopeful that we will not see another surge. We now need to concentrate on the backlog of cancer and elective work that we simply have not been able to prioritise over the past year. It has been incredibly satisfying to begin to see patients coming in for operations they had been booked for over a year ago, and their relief that they may soon be able to get on with their lives is matched only by our delight that our lives, both professionally and personally, may soon return to something resembling normality. Time will tell, of course!

Critics Corner: OMLC Lecture Series

Dr Sarah Ball *(1974 Somerville College), Conservation Geneticist and retired Consultant Paediatric Haematologist*

The Oxford Medical Lecture Club normally meets monthly at Osler House for a lecture on current clinical work and research developments at Oxford. Inevitably, with COVID-19, the lectures have been on Zoom. One glimmer of a silver lining is that this has made accessible a fascinating and erudite series of talks to those of us who would not be able to be there in person. I picked a selection of Zoom lectures, each very different, but sharing a striking common theme of collaboration and cooperation, and the importance of the interface between scientific research and clinical medicine. Not to mention the extraordinary and talented individuals involved. And that includes the Zoom audiences.

"Gene therapy: A Brave New World"
Deborah Gill, Professor of Gene Medicine at the University of Oxford - **bit.ly/OMA-Gill**

This was an absorbing, lucid and informative account of gene-targeted therapeutic approaches in cystic fibrosis, including the ethical implications of gene-editing, and the huge financial costs involved. Professor Gill then broadened the scope of her talk to give an overview of progress in the treatment of other genetic disorders. A mention of the haemoglobinopathies, the "first" single-gene disorders, might have been nice here, given the central role the Oxford group in pioneering clinical and molecular research into genotype:phenotype correlation in sickle cell and the thalassaemias, surely a cornerstone for the contemporary discipline of Gene Medicine. And important also because of their global burden largely affecting third-world countries, begging the question of how to pay the high cost.

"The first hundred days or should it be daze? Surgery in the time of COVID-19"
Neil Mortensen, Professor of Colorectal Surgery at the University of Oxford and President of the Royal College of Surgeons - **bit.ly/OMA-Mortensen**

While July 2020 may not have been the most auspicious time to start his term of office as the incoming President of the RCS, this modestly delivered, matter of fact and often humorous talk reinforced the perception of a chronically under-resourced system, but much more than that, it offered a fascinating insight into the working behind the scenes to juggle the competing needs of the COVID-19 pandemic, emergency and elective surgery, and the massive problem of ensuring effective surgical training. It was refreshing to learn that tackling the high carbon footprint of the OR will feature in new initiatives. We can also hope that this will be the end of the climate of competition as we emerge blinking into the new dawn of augmented reality.

"Apps, wearables and machine learning for the COVID-19 pandemic"
Lionel Tarassenko, Professor of Electrical Engineering at the University of Oxford, and inaugural head of the Institute of Biomedical Engineering (IBME)

COVID-19 was one driving force in the development of a series of clinical devices, for example allowing close but remote monitoring of sick patients while minimising the spread of infection by direct contact, presented in this fascinating lecture by Professor Tarassenko. This was a supreme example of advances resulting from a multidisciplinary approach, in which ingenious engineering solutions are inspired by clinical need.

"Parkinson's Disease: pathological mechanisms to target discovery"
Richard Wade-Martins, Professor of Molecular Neuroscience at the University of Oxford, and head of the Molecular Neurodegeneration Research Laboratory and the Oxford Parkinson's Disease Centre - **bit.ly/OMA-WadeMartins**

This lecture delivered what it said on the tin, but in the form of a brilliant narrative smorgasbord of what can be achieved with multidisciplinary translational neuroscience, using the full gamut of cellular and molecular biology tools, as well as the important input of affected individuals. And bring on Pharma to facilitate the development of drug therapy. This was awesome, a real masterclass. And yes, immunofluorescence should of course be featured on prime-time television.

Memorial Tribute to Professor Peter Sleight (1929 - 2020) - bit.ly/OMA-Sleight

This memorial talk, presented by cardiologist Dr Keith Channon and supplemented by tributes from a veritable roll call of the Oxford medical great and good, celebrated the life and work of an undersung hero with a giant personality and irreverent sense of humour, who inspired admiration and affection in equal part. His eclectic talents ranged from designing Heath Robinson contraptions for barometry to launching the multicentre ISIS clinical trials, the foundation stone of evidence-based clinical cardiology.

If you would like to register your interest for future lectures, please email **oma@medsci.ox.ac.uk**. New members are always welcome and lectures are free to attend.

NEWS AND CONGRATULATIONS

Breakthrough Oxford malaria vaccine shows record efficacy in early trial

A new vaccine against malaria, one of the world's leading causes of child mortality, could be on the horizon as scientists at Oxford's Jenner Institute announce that their candidate achieved 77 per cent efficacy in early stage trials – making it the first malaria vaccine to meet the World Health Organisation's target of 75 per cent. The vaccine - developed by the same lab that worked on AstraZeneca's COVID-19 vaccine – represents a new hope in the global fight against malaria, The Phase IIb trial of the vaccine candidate, R21, enrolled 450 children in Burkina Faso, one of the 10 countries with the highest cases of malaria and subsequent deaths. The vaccine candidate was developed in collaboration with Novavax and the Serum Institute of India (SII). A more extensive Phase III trial is now underway involving 4,800 children aged five to 36 months in four countries. "These significant results support our high expectations for the potential of this vaccine, which included reaching the WHO-stated goal for a malaria vaccine with at least 75 per cent efficacy," said Jenner Institute director, Professor Sir Adrian Hill KBE FMedSci FRCP FRS (1979 Magdalen College). "With the commitment by our commercial partner, Serum Institute of India, to manufacture at least 200 million doses annually in the coming years, we believe this vaccine could have a major public health impact."

Professor Sir Adrian Hill awarded Knighthood and honoured by the Royal Society

Professor Sir Adrian Hill KBE FMedSci FRCP FRS (1979 Magdalen College), Co-Director of the Oxford Martin Programme on Vaccines, received an honorary knighthood for services to Science and Public Health in the 2021 Queen's Birthday Honours list. In May 2021, he was also elected a Fellow at Magdalen, the Lakshmi Mittal and Family Professor of Vaccinology, and founder and Director of the largest academic vaccine centre in the world, the Jenner Institute at the University of Oxford. The Royal Society is a Fellowship of many of the world's most eminent scientists and is the oldest scientific academy in continuous existence.

Dame Sarah Gilbert awarded Damehood and RSA Albert Medal

Dame Sarah Gilbert DBE awarded Dame Commander of the Most Excellent Order of the British Empire (DBE) for services to Science and Public Health in the 2021 Queen's Birthday Honours list. Dame Sarah has also been awarded the Royal Society for Arts, Manufactures and Commerce' (RSA) Albert Medal for her work on the Oxford vaccine. The lead researcher on the Oxford vaccine team, Dame Sarah is Professor of Vaccinology in the Nuffield Department of Medicine at the University of Oxford. She is the Oxford Project Leader for ChAdOx1 nCoV-19, a vaccine against the novel coronavirus, SARSCoV-2, with approval for use in many countries around the world. The RSA Albert Medal is awarded annually to recognise the creativity and innovation of individuals and organisations working to resolve the challenges of our time. Dame Sarah receives the 2021 honour for her services to collaborative innovation for the global common good. She is the 156th recipient of the medal, which was instituted in 1864 as a memorial to Prince Albert, former President of the Society. Previous recipients range from scientists to artists to social campaigners: they include Alexander Graham Bell in 1902 for the invention of the telephone; Marie Curie in 1910 for the discovery of radium; Stephen Hawking in 1999 for improving public awareness of physics; and Tim Berners-Lee in 2002 for the creation of the World Wide Web.

We are proud of the Oxford medical community who received recognition in the 2021 New Year Honours list and 2021 Birthday Honours list. Congratulations to them all.

SIR PETER HORBY, Professor of Emerging Infectious Diseases and Global Health, appointed Knight Bachelor in the 2021 Birthday Honours list for services to Medical Research.

SIR MARTIN LANDRAY FMEDSCI, Professor of Medicine and Epidemiology; Research Director, Health Data Research UK; Deputy Director, Big Data Institute; Lead, Big Data and Computing Innovation, MRC Population Health Research Unit; Lead, Clinical Informatics and Big Data, NIHR Oxford Biomedical Research Centre; Lead, Health Informatics Hub, UK Biobank and Honorary Consultant Physician, Oxford University Hospitals NHS Foundation Trust, appointed Knight Bachelor in the 2021 Birthday Honours list for services to Science and Public Health.

SIR ANDREW POLLARD BSC MBBS PHD (LOND), DIC, MRCP (UK), FHEA, FIDSA, FRCPCH, MA, FMEDSCI, Professor of Paediatric Infection and Immunity, appointed Knight Bachelor in the 2021 Birthday Honours list for services to Public Health.

SIR DAVID STUART FRS FMEDSCI, Nuffield Department of Medicine's Professor of Structural Biology, appointed Knight Bachelor in the 2021 New Year Honours list for services to Medical Research and the Scientific Community.

SIR KEITH WILLETT, Director of Acute Care to NHS England and Professor of Orthopaedic Trauma Surgery, appointed Knight Bachelor in the 2021 Birthday Honours List for services to the NHS.

PROFESSOR TOM SOLOMON CBE (1984 Wadham College), Director of the National Institute for Health Research (NIHR) Health Protection Research Unit in Emerging and Zoonotic Infections, appointed CBE in the 2021 Birthday Honours list for services to Neurological and Emerging Infections Research, including during the COVID-19 response.

PROFESSOR CHRISTOPHER FAIRBURN OBE (1969 Worcester College), Emeritus Professor of Psychiatry, appointed OBE in the 2021 Birthday Honours list for services to Psychological Treatments and the Treatment of Eating Disorders.

PROFESSOR CATHERINE GREEN OBE, Associate Professor in Chromosome Dynamics at the Wellcome Centre for Human Genetics, Senior Research Fellow at Exeter College, and Head of Oxford University's Clinical BioManufacturing Facility, appointed OBE in the 2021 Birthday Honours list for services to Science and Public Health.

PROFESSOR TERESA LAMBE OBE, Associate Professor and investigator at The Jenner Institute, appointed OBE in the 2021 Birthday Honours list for services to Science and Public Health.

PROFESSOR ELEANOR STRIDE OBE, Statutory Professor of Biomaterials in the Departments of Engineering Science and NDORMS, appointed OBE in the 2021 New Year Honours list for services to Engineering.

We also congratulate **DR GARETH HYNES MBE,** Specialist Registrar in Respiratory Medicine, at Oxford University Hospitals and a Clinical Research Fellow at the University of Oxford, who was awarded MBE in the 2021 New Year Honours list for services to Medical Education during the COVID-19 pandemic.

And in other news...

PROFESSOR ERVIN FODOR (1992 Worcester College) and **PROFESSOR ROBERT KLOSE,** are two of 64 life scientists to be elected to The European Molecular Biology Organization (EMBO).

DR LENNARD LEE (2005 Queen's College) has been awarded ACP McElwain Prize for contributions to medical oncology during the COVID-19 pandemic, through the establishment of the UK Coronavirus Cancer Monitoring Project.

DR EOGHAN MULHOLLAND, Postdoctoral Research Scientist in Cancer Genetics at the Wellcome Centre for Human Genetics has recently been awarded the Lee Placito Research Fellowship in Gastrointestinal Cancer.

PROFESSOR JONATHAN REES, The Nuffield Department of Orthopaedic, Rheumatology and Musculoskeletal Sciences (NDORMS), has been appointed as the new Director of the Botnar Research Institute.

PROFESSOR ANDI ROY leads one of the five research teams across the UK that have been awarded the 2021 Cancer Research UK-Children with Cancer UK Innovation Award to develop new treatments for childhood cancer.

Dr Jean Smellie (died 14 September 2020)

It is with great sadness that we learn of the death of Dr Jean Smellie (1944 St Hugh's College), aged 93, a distinguished paediatrician who specialised in the management of children with urinary infection. Her meticulous research was important in developing our current understanding of the condition and substantially reducing the number of investigations and operations to which children were subjected.

Excerpts from Recollecting Oxford Medicine Interview of 2014. Jean speaks about her life in her own words.

What made you decide on Medicine for a career?

At school (all girls), it was generally reckoned that if you were bright you did medicine, if you were moderately bright you became a physiotherapist or something, and if you weren't you became a Land Girl.

What are your earliest memories of Oxford?

Because St Hugh's had the Head Injuries hospital we were distributed around Oxford, nominally to New College but I was in Balliol's Holywell Manor... There were 10 women out of the 50 medical students. The men were either straight from school or had a disability that made them unfit for military service.

So how did your first years go?

The anatomy department was busy and friendly. Alice Carlton taught brilliantly, humorous but exacting, with her flashing eyes and hair blued on Fridays. 'Converge, converge' was her expression if attention wasn't paid to her blackboard drawings. Professor Wilfred Le Gros Clerk was a lovely man, benign and more of a physiologist than a stickler for the small print in Jamieson's Anatomy...

And how about life outside the departments?

There were numerous societies. Margaret Roberts (Thatcher) was secretary of the Conservative Society then, and she invited distinguished politicians. The Union debates were usually good (ladies were confined to the gallery) and Anthony Wedgewood Benn was an active member. And there was time for non-medical lectures, such as Lord David Cecil's on 18th and 19th century novelists and Kenneth Clark's lectures at Ruskin College.

And then you'd have come to your third year.

During the War, there were two-year BA intakes. We were six female and six male, together with six who did a two-year BA previously but now returned. For me, this was the most formative and informative year ('46-'47). I had neurology tutorials with Whitteridge, but I was scared stiff of him. Liddell was Professor of Physiology, and in a practical demonstration, with cats, you had to stand clear as he could easily launch a scalpel across the room, just getting it off his chest.

Then you'd have gone on to your clinical work.

I'd been up to London at the end of my first year, when the buzz-bombs were around, to secure a place at one of the four London hospitals taking women (and this soon dropped to three, when the West London fell out). Luckily UCH accepted me, and on entry there were again 10 women out of 50, but a mix of London, Oxford and Cambridge students. Exams were all held back in Oxford.

So when did you come to work clinically in Oxford?

In 1960, I was appointed to a Lectureship in Professor Witts' Nuffield Department, though it was in Paediatrics, and it was before the full development of the Oxford clinical school. We worked on two sites, the Radcliffe Infirmary and the Churchill (a wartime Canadian hospital in Nissan huts), but also linked with peripheral hospitals Banbury and Abingdon out-patient clinics. And in Oxford I had my first car, 10 years after qualifying, and I had an official day off, for the first time ever! The neonatal service was good, and there were good relationships with most departments. I was establishing an interest in metabolic diseases that presented to the Wingfield-Morris Orthopaedic hospital, and then there were the families in Brill where there'd been a lot of in-breeding; it grieved me that were all sorts of diseases unexplored and all the brains in the world to explore them.

And did you see anything of the adult physicians such as Pickering?

Well, he was a man after my own heart. I first met him when I was going to do my DM thesis on chests, and John Hodson at UCH was keen on the radiology of the people who lived around King's Cross, with the smog and the railway smoke. I'd done the chest expansion with a tape measure, and Pickering thought this was great, and accepted it as the stuff for a DM thesis. But that didn't get written, but a DM came later from published works on urinary reflux, urinary infections and renal involvement.

The interview with Dr Jean Smellie is available here: **www.podcasts.ox.ac.uk/series/recollecting-oxford-medicine-oral-histories**

Dr John Spalding (died 13 February 2020)

As we reported in the last edition of *Oxford Medicine*, Dr John Spalding (1936 New College) died on 13 February 2020. Dr Spalding was a well respected consultant and research neurologist for Oxford United Hospitals.

Here we include extracts compiled by Dr Derek Hockaday (1947 Brasenose College) from Dr John Oxbury's (1972 Christ Church) interview of Dr John Spalding. You can also listen to John on the following podcast: www.podcasts.ox.ac.uk/interview-john-spalding-former-consultant-and-research-neurologist-oxford-united-hospitals

I believe you started your career in neurology by being a student house officer for Cairns at the Radcliffe Infirmary (RI) during the Second World War.

Indeed. I was a student house surgeon for Hugh Cairns because nearly all the young doctors were in the forces so there were no registrars and the few remaining qualified housemen had to cope with two firms each. At the time, Cairns was to a large extent concerned with the Military Hospital for Head Injuries which he'd established at St Hugh's College. He very kindly became my medical adviser, and recommended I did neurological house jobs, as with Russell Brain and Douglas MacAlpine in London. Then he told me Ritchie Russell, who had worked at St Hugh's, needed an assistant in Oxford.

After the War, Ritchie, Charles Whitty and I all worked on the punch cards and original notes from all the patients with penetrating head injuries who'd been treated at St Hugh's or subsequently, with the moves of the Head Injuries Hospital, at Headington Hill Hall or later Wheatley. Ritchie had created the punch cards, described by one colleague as Ritchie's folly, but they proved invaluable and were the basis of a great many publications. Ritchie put me onto localised injuries of the visual radiation and visual cortex. Gordon Holmes, from the First World War, had emphasised that the upper and lower parts of the radiation were distinct, but I was able to show that the radiation was a continuous sheet and to demonstrate the visual defect that resulted from injury to the intermediate section. And I could give more detail to representation of the visual field in the cortex.

When Ritchie started he lacked beds in Oxford, and used some in Stoke Mandeville Hospital 20 miles away. But more important was the lack of facilities for proper investigation of neurological patients. Professor Witts, Nuffield Professor, had some beds at the Churchill as well as his main wards at the RI, and arranged for Ritchie to have use of four of these for patients requiring air encephalograms, angiograms and myelograms. Ritchie's patient load meant that six beds were really needed, so there was a panic to explain bed allocation on the rare occasions when Witts himself did a ward round there.

Stoke was towards Aylesbury where there was an outbreak of polio. At the time, patients with their respiratory muscles involved were sent to infectious disease hospitals which had neither the staff nor experience to treat them. Ritchie decided to take them on, using tank respirators, as everyone did then. These had the body in a tank, with an air-tight seal round the neck, and bellows that sucked the air out of the tank around 18 times a minute, so drawing air into the lungs. It provided satisfactory respiration but many patients also had difficulty in swallowing, so saliva pooled in the mouth and was fatally sucked into the lungs. About 1951, Lassen in Denmark saw the similarity to curarized patients, and intubated patients to connect them to an anaesthetic machine which supplied air if a medical student squeezed the bag. Ritchie asked help from Edgar Schuster, originally an MRC administrator who became a skilled instrumentalist during the War, and he produced the 'East-Radcliffe Respirator' to push the air in and out automatically. John Marshall and I added a hot water humidifier to prevent secretions forming crusts which were difficult to suck out.

As other neurological conditions may need artificial ventilation, a Respiration Unit was built opposite Ward 13 with eight respirators.

It must have been very exciting when you extended the diagnoses you were treating to Guillain-Barre, myasthenia gravis and tetanus.

Yes. The severe tetanus patients could neither breathe nor swallow, so we treated them with curare to break the spasm of their voluntary muscles, but then of course they needed ventilation.

And I believe they had complications from autonomic nervous system involvement.

Yes, they and the Guillain-Barre patients had trouble with blood pressure control. In the latter it was often too low, which was easily treated by lowering the head of the bed. But the tetanus patients were liable to hypertension, such as 240/140 mmHg, as the toxin inhibited the normal inhibitions of vascular contraction. Fortunately, beta blockers were just coming onto the market, and worked well. There was also excessive sweating and we had to work hard to get the patient's fluid balance right.

And we had the facilities to look at other autonomic problems such as orthostatic hypotension; David Oppenheimer, neuropathologist, showed that in the spinal cord preganglionic sympathetic cells and their fibres had disappeared, and there was also damage to cerebellar connections. We published these findings under the title 'Multiple System Disease'.

There was an interesting interlude through an outbreak of paralysis in Morocco. It was severe enough to prevent walking, and affected hundreds daily. Ritchie, as an expert on polio, was contacted, and he asked Honor Smith and I to go. It was soon clear that it wasn't infectious, but there was a suspicion of a toxic cooking oil. Fortunately, one of Honor's brothers was Chairman of Shell, so she was able to send samples to their laboratories. They quickly identified many as expensive aero engine oil. It turned out that when the Americans had closed an air base, they didn't take away the stock of engine oil, but sold it as lubricating oil; but there was a lot of it and the market for lubricant was limited, so the initial purchasers sold it on as cooking oil. Unfortunately, it contained ortho-cresyl phosphate which makes engine oil resistant to the very high temperatures in aero engines, but was also known to cause paralysis if swallowed, as had happened when it was included in 'Ginger Jake', something marketed during 1920's prohibition in the USA.

How long were you and Honor in Morocco?

We stayed as long as necessary, which was about a week.

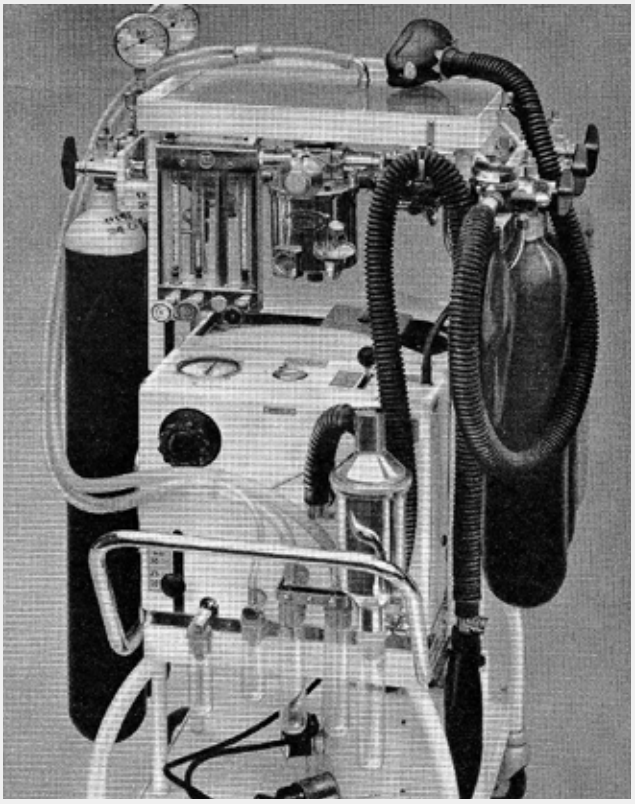
Incredible that you cracked it in so short a time. Now, I know that you published about 100 papers and at the same time you were working as a busy general neurologist in Oxford and also Northampton. How did you successfully combine all this?

It was something that was fun to do. It was very interesting. And we had a succession of very able post-graduate students who did a huge amount of the work. There was Lionel Opie, who went on to work with Hans Krebs and then into cardiology in his native South Africa. There were Harold Rotman and John Corbett, who had successful careers on return to the USA and Australia respectively. There was also Bill Watson who became Professor of Physiology in Edinburgh and has sadly now died, as did Ralph Johnson from the bees he started to keep in retirement from clinical work. Chris Mathias from India did a lot of work on autonomic activity in paraplegics and tetraplegics and went on to join Roger Bannister at St Mary's and at Queen Square.

You published a book with Ralph Johnson.

That was 'Disorders of the Autonomic Nervous System'. We also wrote one on the autonomic system and the alimentary tract, and I had co-authored two earlier books on artificial respiration.

It's fascinating, John. I knew a lot of the things you've done but it's clear that there's an enormous amount I didn't know.



East-Radcliffe Respirator designed to help polio patients breathe. Extended to treat patients with severe tetanus. The forerunner of modern anaesthetic ventilator.

St Hugh's College Dining Hall as a head injury ward during World War Two.

Obituaries

PROFESSOR JANE MELLANBY (1938 – 2021)

Written by two of Professor Mellanby's children - Lawrence Impey (1982 St Peter's College), Consultant in Obstetrics and Fetal Medicine, Oxford University Hospitals NHS Foundation Trust, and Harriet Fitski (née Impey).

Generations of Oxford medical students, including those from her own college St Hilda's, will remember 'Dr Mellanby'. If it was not her blunt approach, her challenging tutorials, garden parties or seminars at her house, or the prize for finishing her biochemistry practical first (a quantity of beer), it was for advancing the cause of women in medicine and science. 'Dr Mellanby's greatest gift to me', wrote one of her students, 'was to both fearlessly champion me and to tell me in no uncertain terms when I'd been an idiot.' Often unorthodox in her selection and with a determination to help potential students from less privileged backgrounds, she inspired first fear and then fierce loyalty and love. It was as an 'outstanding and inspirational educator of female medical students' that she was elected to an Honorary Fellowship of The Royal College of Physicians in 2016, and in later years it was her students, she felt, that were her most important legacy.

Born in Sheffield in 1938 into a scientific family, Mellanby was always determined to follow in their footsteps. As an only child in wartime, she endured evacuation at the age of two and the divorce of her parents. She had to attend science A-level classes at a neighbouring boys school because physics and chemistry were not even taught at her girls' school, which may well have contributed both to her passionate support of women in science, and to her support of her students, as although brilliant she was a difficult pupil herself.

In 1956 she went up to Somerville College, Oxford, to read Botany, Physiology and Chemistry. This was followed by a D.Phil. on intermediary metabolism with Nobel scientist Sir Hans Krebs. She began as a neurochemist, working with tetanus toxin and botulinum toxin as a Research Associate at the Sir William Dunn School of Pathology, and with Professor Larry Weizkranz she went on to set up a Neurochemistry unit in the new Department of Experimental Psychology where, among other things, she developed a seminal animal of epilepsy.

Ignoring Krebs' advice that marriage would 'end her career', in 1961 she married Oliver Impey, whom she had met drawing an aspidistra in a botany practical, and to whom she was happily married for more than 40 years until his death in 2005. They had four children, and combining it all was a battle, especially given the societal attitudes of the time. Television was banned (she never owned one), the children were instilled with a deep seated sense of rebellion but her extraordinary energy and determination were applied to her family too. She was a committed Christian, finding this entirely compatible with her knowledge of science and medicine.

From 1971, Mellanby had a Tutorial fellowship at St Hilda's, and her flair as a teacher and mentor was able to develop fully, as well as her interest in the issues of the college and the university. She fulfilled many other roles including Vice-Principal and Tutor for Admissions, and was a passionate supporter of the college staying women-only. The principal reason she gave was that in having to 'incubate' children, women's research output would be disadvantaged. The college voted to admit men shortly after her official retirement.

In the 1990s, her focus began to shift towards education, in particular the socio-economic disparities in performance and identification of under-achieving students and children. Her research on why women appeared to fare less well academically at Oxford, made headlines. As governor of a local comprehensive school, she was told there were 'no clever children', a statement she rapidly disproved. Her team developed VESPARCH, a verbal and spatial reasoning test to tackle the bias within contemporary standardised tests against underprivileged children. A generation of pre clinical and psychology students contributed with dissertations, going to the school and then many others, testing children and honing the performance of the test and examining the importance of grammar. In 2014, at 74, she published her book 'Education and Learning – an evidence-based approach'. This work, in collaboration with Cambridge Assessment, is set to have a lasting impact on the approach to underachievement in the UK, and will continue to influence our education system in the future.

Right to the end of her life, Mellanby continued to work, swim every morning, garden, supervise students, paint, cook enormous meals, chair endless committees and see her family and many friends. 'There are,' she would say, 'just so many things that need doing.' One might argue that during her 82 years Jane Mellanby managed to do most of them.

Jane Mellanby died on 8th February 2021. A memorial service for later in the year is planned.

Obituary in *The Times*: www.thetimes.co.uk/article/professor-jane-mellanby-obituary-27fdhsn0r

DR DAVID CUTHBERTSON WEIR (1956 - 2020)

Dr David Weir (1975 Corpus Christi College), Respiratory Consultant.

he knows not where he is going
For the oceans will decide
It's not the destination
It's the glory of the ride..."
- Edward Monkton

David's passion was medicine, all things respiratory from sleep medicine to malignancies and all things lung in between.

From his early Oxford study, to his finishing in Edinburgh, this shy argumentative Mancunian carved a career across many countries laterally choosing to return to his early roots in the north of Manchester where he worked as a respiratory consultant. He was known as a great leader and educationalist, renowned throughout the whole of Greater Manchester and Europe for his potential led research into COPD, improving the lives of patients and supporting other would be medics to do the same.

His dislike of bureaucracy was both a blessing and a curse as he relentlessly campaigned for improved healthcare for his beloved patients in the surroundings of his workplace.

His Oxford rugby and rowing days stood him in good stead for his hiking across his beloved Scottish mountains, always with a dog or two in tow and in the last few years, his home on the West Yorkshire moorland provided him with an endless landscape to roam.

His early culinary diet of port and Garibaldi biscuits (ahh.. the student life) progressed to a love of all things grape and foodie, preferring to grow his own produce, making jams, baking bread in his attempt to create his own version of the good life.

He worked right up until he left our lives doing the job he loved and will be greatly missed by all who knew him.

His wife, Jane

DAME FIONA CALDICOTT DBE, FMEDSCI (1941 - 2021)

We are sad to report that Dame Fiona Caldicott (1960 St Hilda's College), former Principal of Somerville College (1996 to 2010), died on 15th February 2021. Dame Fiona is perhaps best-known for the role she played in developing the Caldicott Principles, which govern the use of patient information within the NHS. Since the publication of the Caldicott Report in 1997, the Caldicott Principles have become indispensable tools for managing personal confidential data, with over 22,000 Caldicott Guardians appointed not only within the NHS, but also in prisons, the Ministry of Defence, the police and overseas. Having already served as the first female president of the Royal College of Psychiatrists and the chair of the Academy of Medical Royal Colleges, Dame Fiona's career encompassed many other positions of high office, including as Pro Vice-Chancellor of Oxford University and Chair of Oxford University Hospitals NHS Trust.

Obituary in *The Guardian*: www.theguardian.com/politics/2021/mar/17/dame-fiona-caldicott-obituary

SIR PETER HARPER (1939 - 2021)

Sir Peter Harper (1957 Exeter College) was a world expert on the genetics of inherited neurological disorders, particularly Huntington's disease and muscular dystrophy. He also advocated the idea of genetic counselling – helping people to understand the implications of inherited disorders that might affect them and their families. Finding a genetic link between the two wasting conditions has led to highly accurate diagnostic and predictive tests for at-risk individuals and their families. Peter played a leading role in that discovery, and in establishing that in both disorders genes have unstable DNA sequences that tend to expand over generations, accounting for the phenomenon of "anticipation", by which both conditions worsen, and occur at an earlier age, in successive generations. While there is still no remedy, his work has contributed to an understanding of the underlying molecular mechanisms, providing hope that a cure will one day be available.

Obituary in *The Guardian:* www.theguardian.com/science/2021/feb/15/sir-peter-harper-obituary

PROFESSOR BRYAN SYKES (1947 – 2020)

Professor Bryan Sykes, the human geneticist who proposed that 95 per cent of Europeans could trace their ancestry to one of seven women living thousands of years ago, has sadly died at the age of 73. Professor Sykes pushed forward the analysis of inherited conditions, such as brittle bone disease and double-jointedness, and was one of the first to extract DNA from ancient bone. The same Bryan Sykes, holder of a personal chair at Oxford University, analysed hair supposedly taken from mythical hominids such as the Bigfoot and Yeti, and announced the results in a three-part television series. His delight in science and enthusiasm for communicating it to popular audiences were both aspects of an expansive personality that alternately inspired and exasperated his colleagues.

Obituary in *The Guardian:* www.theguardian.com/science/2020/dec/18/bryan-sykes-obituary

DR GRANT DE JERSEY LEE (1921 – 2021)

Dr Grant Lee (1958 Pembroke College), retired consultant cardiologist, died peacefully on 3rd May 2021 age 99.

An interview with Dr Lee can be heard here: www.podcasts.ox.ac.uk/series/recollecting-oxford-medicine-oral-histories

In Memoriam

Dr Jeffrey Bissenden *died 10 July 2020*
(1963 Pembroke College)

Alviar Cohen *died 21 June 2021*
(2020 St John's College)

Prof John Dupre *died 30 December 2020*
(1950 St John's College)

Dr David Emerson *died 03 December 2020*
(1952 Lincoln College)

Dr Helen Foley MBE *died 31 January 2021*
(1955 St Hilda's College)

Dr Richard Greenhall *died June 2021*
(Consultant Neurologist)

Prof Robert Hill *died 16 January 2021*
(1944 New College)

Dr Michael Kelly *died 20 June 2020*
(1949 Trinity College)

Dr Jacqueline Livsey *died 04 October 2020*
(1988 Merton College)

Dr John Manners *died 20 July 2020*
(1953 Wadham College)

Prof Don Mason *died 03 January 2021*
(1968 St John's College)

Dr Elizabeth Maughan *died 23 October 2020*
(1985 Pembroke College)

Dr Andrew Pengelly *died 25 March 2021*
(1961 Keble College)

Dr Jane Sampson *died 24 January 2021*
(1942 St Hugh's College)

Dr Robin Wallace *died 20 March 2021*
(1955 Exeter College)

Dr James Wigdahl *died 16 January 2021*
(1948 Magdalen College)

Please contact the OMA team (**oma@medsci.ox.ac.uk**) regarding any obituaries of friends or colleagues you would like to be considered for entry into the next edition of *Oxford Medicine* (December 2021).

Kelp Violins

Dr Roger Bodley
(1966 Worcester College), retired Radiologist

Following a concert is the local tulip fields of NW Tasmania, featuring violin music inspired by undulating Bull Kelp movements in the local seas, I thought it might be possible to make a violin body from the wide fronds of the kelp.

Kelp has long been used by Indigenous Australians for baskets, food carriers and trinkets and now has a more widespread use as a food, soil fertiliser, biopolymer source and additive for cattle feed to decrease the methane production from rumination. We could not find references to its use as an instrument making material.

Problems were overcome by trial and error. My first violin shrank to half the size as it dried and hardened! A medical mishap led me to store several fronds in the freezer to preserve them from their usual rapid, repulsive decomposition. When I came back to work on them I found that they were encased in solid ice and that they had been effectively desiccated and had a texture like thick leather.

Two different approaches have created very attractive instruments that have a beautiful and surprisingly strong tone and volume:

Enlarged violin shapes are cut from the fresh kelp and frozen to desiccate them until no further ice forms, by which time they have shrunk to most but not all of their final shape and size. As they dry and shrink further in clamps, they come to behave like a rigid thermoplastic material and, using a hot air gun, can be softened, cut and moulded into new shapes relatively easily.

Kelp edges cannot be glued securely, so I have used waxed hemp thread to sew the body plates and sides together around a central wooden spine that takes the tension of the strings. This construction method is a complicated process

The first five violins – I gradually overcame the problems of shrinkage.

that called on skills learned in pelvic and plastic surgery junior doctor jobs and interventional radiology honed dexterity.

A friend, Dr Chris Henderson's approach has been to use a more traditional construction method with internal wooden bouts but with an aluminium or carbon fibre tube spine and to screw and mastic the plates, bouts and walls together.

F holes would weaken the front plate in both violins so other holes were cut to emphasise the different frequencies. In both designs, sound posts were thought to be of doubtful benefit as the kelp appears to have little inherent resonance but the arched front and back plates are prevented from collapsing (an early complication) by spacers around the spine.

The violins look interesting and attractive and have been very well received musically, despite the current strings being fairly cheap and of low quality as these are "proof of concept" projects.

They have already been presented and played at a seminar of a group of seaweed researchers in The Institute of Marine and Antarctic Studies, Hobart, and will feature in an International Symposium on Seaweed in IMAS early next year.

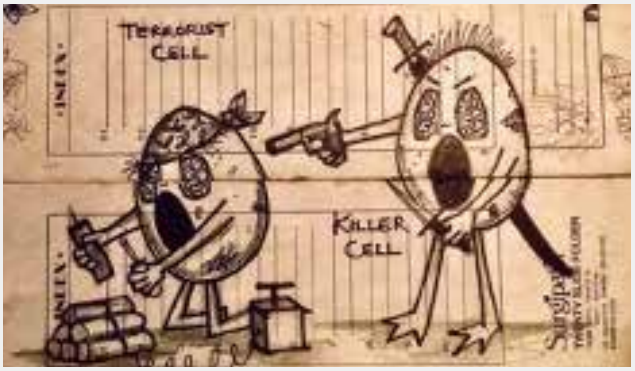
Videos of kelp underwater and kelp violin playing:
bit.ly/OMA-WestPointKelp
bit.ly/OMA-ES-Violin

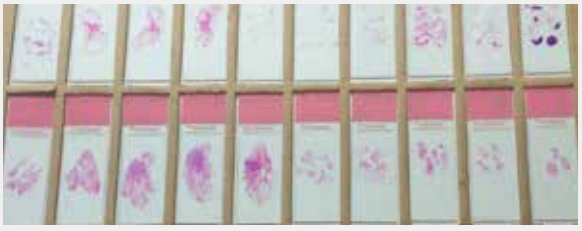
Kelp Violin and Underwater video courtesy of Emily Sheppard.

Slide Tray Art

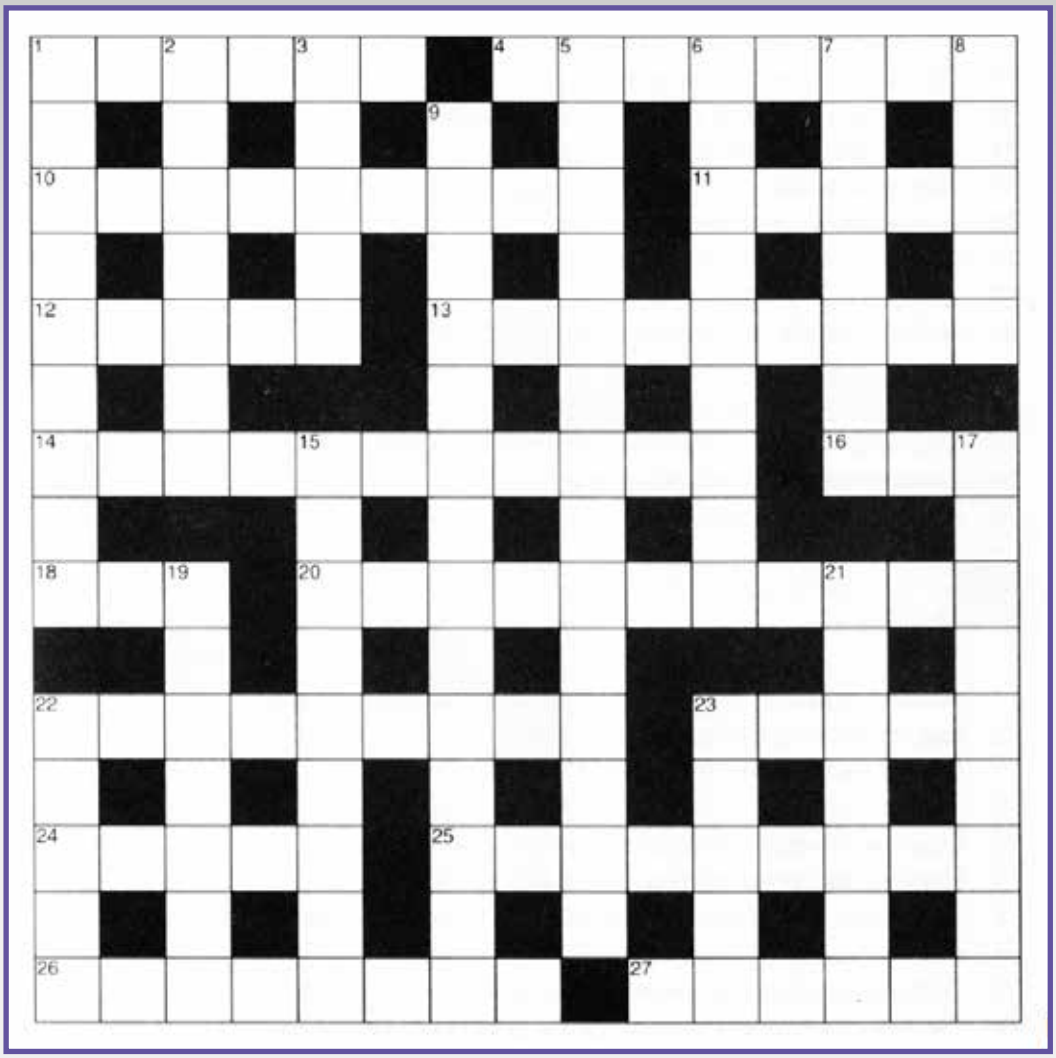
Dr Chris Mason
(1977 Worcester College), Consultant Histopathologist, Exeter

"You may be wondering why these cartoon/drawings are so random!? Let me explain... These pictures started life as doodles on Histology slide trays - done during those occasional moments of contemplation that punctuate the working day of every histopathologist (!?!). The shapes of pre-existing marks and blemishes were initially used as the inspiration for a drawing, however this soon progressed into a more planned and adventurous 'artistic'(???) process. Please enjoy..."





Crossword



ACROSS

1 Cut in dimensions reportedly (6)
4 I'd lace it to make it like an intestinal surface (8)
10 More than one up your sleeve? (3,6)
11 Sense disorderly state (5)
12 Abbreviated speciality sounds to have space (5)
13 Sometimes shaved, so not enough weapons (9)
14 Communicate without energy to the skilled and refractory (11)
16 Pat bad back (3)
18 By the sound of it, Asian national draw (3)
20 Juvenile school taxi back late endlessly (11)
22 Not medicals, University crush garlic in the ship (9)
23 Tube found in first entrance (5)
24 Boat has time after achy mix-up (5)
25 Pioneer at home with no gold after tax (9)
26 Controlling the course of second peg band (8)
27 Reload terrible nightmare (6)

DOWN

1 Physician sees fashionable flier (9)
2 Nearest little room where son hides (7)
3 Points to strange part of blood (5)
5 Home team beat sub I ring for internal damage (6,8)
6 Step in to move vine tree round the pole (9)
7 Stunned by disorganised Easter Day at first (7)
8 Outfit for doctor on Eastern ship (5)
9 Search everywhere to make a cleaner Britain (5,3,6)
15 A dog keeps quiet for man giving out the post (9)
17 Table rail gets fitted both sides (9)
19 Ace hare boxing could give you this (7)
21 Where surgeons perform? (7)
22 Eye problems where pigs live reportedly (5)
23 Cut off point always (5)

Mr David Williamson
(1974 Corpus Christi College), Consultant Orthopaedic Surgeon, Swindon

Dean of Degrees

Peggy Frith *MD FRCP, New College Dean of Degrees*

Over the past several summers, I have been pleased to act in loco Regius Professor of Medicine at the Sheldonian degree ceremony. I proudly present all the medics who are finally graduating as qualified doctors. It's always a splendid day, usually with fine summer weather, happy students, celebratory parents, family and friends, and jollities in the colleges afterwards. It is a piece of theatre, a chance to dress up, and I put on the scarlet robes of an MD to 'big-up' for the occasion. There is a routine and a formula - literally the Latin intonation recited to the VC and Proctors : 'Insignissime Vice Cancellaria ...'. Graduands pledge their loyalty to uphold the University's reputation, and college Deans compete in how well they indoctrinate their flock exactly when, and how loudly, to shout together their 'Do Fidem!'. There are sometimes incidents of incorrect dress – no brown shoes, pale tights, unwelcome handbags or conspicuous jewellery, so that it is all fully 'sub-fusc, below-the-brown'. Sometimes there are extra twists to the day. One year, an elderly Dean quietly collapsed in his chair and the observant VC had to signal to those Deans who might have some skills to revive him. The Sheldonian does have a defibrillator in a cupboard, and now also has a canvas stretcher, so we can exit the stage promptly if we need to get to work in a more dramatic way than for a simple faint. I hope that we meet again in July 2021 to launch the next group of students. 'Troops over the top', into the real world, ready for action.

Painting a Pandemic: Osler House Art Competition

Dervla Carol
(2015 St Anne's College)

The end of the first wave lent itself to reflecting on the experiences of the COVID-19 cohort. July stretched to a more liberated August – but the hospital was quiet. We debated a second wave - back to normal by Michaelmas, of course.

Of course – the next swell of the pandemic rolled into the autumn. It felt important for Osler House to tangibly acknowledge the experiences of medical students in a way which all members of the student body could relate to.

We created a competition open to all NHS staff and healthcare students. Entrants were asked to use artwork to commemorate the COVID-19 generation in a way that was sensitive to all experiences of the pandemic. Five very diverse entries were shortlisted and Matthew Gowell, portrait artist and final year medical student at Oxford, was voted the winning entrant with beautifully detailed examples of his previous work.

Due to COVID-19 restrictions, it has been over a year since I have been able to enter Osler House. When I can return, I hope this piece will be showcased to allow everyone who has been absent feel like their experience has been remembered.

FRONT COVER:
Dr Peggy Frith, Retired Consultant Opthalmologist and former President of the Oxford Medical Alumni

ANSWERS TO CROSSWORD

ACROSS
1. Incise
4. Ciliated
10. Two tricks
11. Taste
12. Rheum
13. Underarms
14. Intractable
16. Dab
18. Tie
20. Prepuberal
22. Surgicals
23. Stent
24. Yacht
25. Innovator
26. Steering
27. Ordeal

DOWN
1. Internist
2. Closest
3. Serum
5. Inside bruising
6. Intervene
7. Tasted
8. Dress
9. Scour the nation
15. Appointer
17. Bilateral
19. Earache
21. Theatre
22. Styes
23. Sever

Poems

BLOOMIN ZOOMIN'

And what about the meeting, to
be held right here, today?
Just when, from mass statistics,
You thought you'd gone away.

Thanks to some genius, it can
be right here in your room,
seen, heard and sweetly spoken
with that intervention, Zoom.

It really should be flaming June
but the roses aren't out, yet.
Some briar buds are already brown
in the relentless wet.

Petals of wind-blown tulips fall,
hide low in hazy gloom.
Take up the numbers' challenge - get
Bright gatherings from Zoom.

Dr Carole Robertson
(1952 Lady Margaret Hall), Retired

THINGS THAT MEDICAL STUDENTS DO: GET SMASHED

G- getting things wrong
E- exasperating patients
T- trying to take bloods

S- sleeping past our alarms
M- moaning about... everything
A- asking stupid questions
S- stressing about exams
H- holding the retractors
E- escaping the ward for "teaching"
D- doing our best

Lisa Li (2013 St Anne's College)
Rosie Lynch (2017 LMH)
Irene Mathias (2017 Christ Church)
Lucy Denlys (2017 St John's College)

HOPE, HEALTH AND HAPPINESS

To the doctors and nurses on the front line

Emerging from darkness, from death and despair
You longed for some lightness to live without care.
From long hours of treating the sick and the dying
You just kept on going - not complaining or crying.

Now we look back at the year that has passed
With more knowledge and hindsight, we still feel aghast.
Tardy decisions and dithering fools,
The vaccine deniers, those flouting the rules

The conspiracy theorists, the Goings of Cummings
Hancock's half measures and Boris's bumblings-
We must look to the future and plan to move on
Get our lives back to normal and now have some fun!

Shop for frivolities, eat out, share a joke
Summer is here, we can party, meet folk,
See family, go clubbing or dating. Be free-
Let the world see you smiling- without PPE!

Dr Lesley Starr
(1976 St Anne's College),
Retired General Practitioner

HAIKU - CLINICAL SKILLS TEACHING

Frustrated with yet
Another missed cannula
I curse the fake arm

Lucy Denlys
(2017 St John's College)

Written on a rainy afternoon at the end of May, these short poems reflect first-time experiences for three generations of Oxford Medical women.

Carole Robertson's first Zoom experience;
Lesley Starr's post-pandemic glimmer of hope and
Year 4 Medical Students' first day at GWH Swindon.

Osler House Boat Club News

Jennifer Holmes
(2018 St Hugh's College), OHBC Alumni Officer

Osler House Boat Club ended our first year on a high, winning double blades at summer torpids! We could not have asked for a better result, with two out of three crews qualifying, and medics of all different abilities competing from Katherine Maitland and Oriane Grant, fresh from the Oxford boat races to novices who only started this September. There was a nervous start to the week as the draw was announced and it was revealed that our W2 boat would in fact be chasing our W1 boat. However, the crews did not let this faze them and stepped up, with W1 getting a bump after an average of 18 strokes and W2 then powering through to get the overbump each day. They both bumped Catz, Trinity, Brasenose and Wolfson showing the world of Oxford college rowing that Osler House means business.

> *"...W1 bumped after an average of 18 strokes... W2 powered through to get an overbump each day!.*

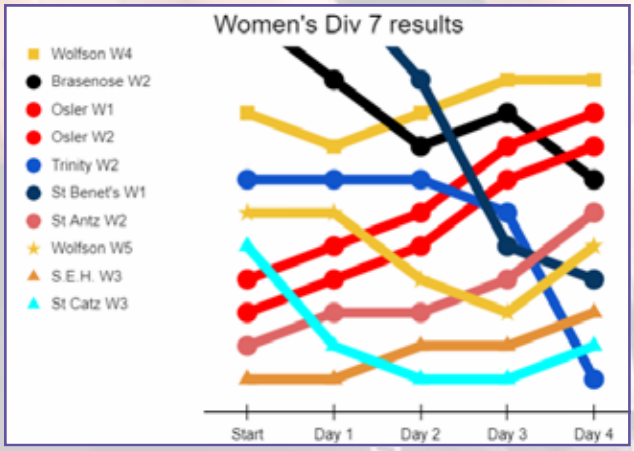
This year was a spectator free event, however there was a livestream, now uploaded to First Sight Media's YouTube if you would like to relive the action! The Osler Boats race at 12.25pm each day. **www.youtube.com/user/FirstSightMedia/videos?view=0&sort=dd&shelf_id=0**

If you want to support the Club further, why not donate for and help us get closer to our goal of getting a new boat for OHBC so even more medics can race in bumps next year.

Opportunities for Alumni to Row

As COVID-19 regulations relax, we are excited to announce the opportunity for alumni to get back in the boat, in collaboration with Oxford Medical alumni weekends. This will start with the 40th anniversary weekend on 31st July - any alumni of OHBC who would like to spend an afternoon back on the Isis river, please do get in touch - we would love to see you!

Please email oslerhousebc.president@gmail.com.
Our GoFundMe page is www.gf.me/u/zcf4kp



Education for Sustainable Healthcare

Hannah Chase
(2018, Green Templeton College) Third-Year Graduate Entry Medical Student in conversation with Dr Lyn Williamson

What is ESH and why is it important?

Climate change is the greatest threat to health this century – that means us, right now. Education for Sustainable Healthcare (ESH) is teaching about the impacts climate change has on health and the sustainability of healthcare systems. It provides students with the skills required to communicate and drive change.

The pandemic has dominated the world for over a year and there is clear evidence pandemics are linked to climate change with predictions they will occur more frequently in the future. Furthermore, the NHS currently has the same global warming effect as the entirety of Estonia, so doctors need to sit up and acknowledge that by ignoring the issue they are actually causing patient harm. Overall, ESH is vital so doctors have the confidence to question, communicate and act, rather than stand by and allow the status quo until it is too late. The net-zero NHS by 2040 commitment is a powerful target and motivator.

What made you interested?

Prior to medical school, I used to be a vet and climate change felt very current and visible, such as changing disease patterns - not something theoretical in the future. At medical school I was struck by the lack of conversation about climate change and was shocked by the ignorance of some colleagues on the topic, rejecting the idea it would impact them or their patients in their lifetime.

How did you start initiating changes?

We hosted two faculty-wide workshops to inspire and kick start curriculum transformation - it is vital ESH is an incorporated theme rather than a stand-alone lecture as it's integral to every speciality. Meanwhile, I also became co-director of an international initiative called the Planetary Health Report Card (PHRC). New to the UK, it assesses medical school engagement in planetary health.

I expect this was not easy. What barriers have you faced?

Initial responses to emails to faculty were quite 'vanilla' but once I made contact with Dr Richard Harrington, graduate medicine course associate director, it has gone from strength to strength - the enthusiasm from him has been phenomenal. However, there are still some, who work in key areas, who have not engaged or resistant to concepts, such as juniors deciding to reduce unnecessary tests.

What have been the 'wins' so far?

Some faculty members have been exceptionally fast at making changes to their course and there are many more promises for next year. Just a couple of examples include Dr Michele Peters changing every lecture in her sociology course to maximise relevant ESH content and Dr Jane Moore overhauling the women's health curriculum to ensure ESH is integral to that rotation. The clinical skills lab has also been transformed to have a sustainability lens on all aspects including green fake blood as a visual cue! In the PHRC (www.phreportcard.org), Oxford came 20th out of 30 UK medical schools. Used to being top of league tables, this is an alien feeling for Oxford medical school and certainly another motivator.

> *"...the NHS has the same global warming effect as the entirity of Estonia...*

Could you give some practical examples of how doctors working day to day in the NHS could make positive changes?

1. Since February 2020, NHS England have used over three BILLION aprons and facemasks. There are now hospital grade reusable ones eg Revolution-ZERO so why not use them - is it just convenience?

2. Inhalers make up approximately four per cent of the NHS carbon footprint. Changing from MDI to DPI inhalers where possible is a simple way we can collectively make a huge difference (two per cent reduction with a 50 per cent switch).

3. I think the most important thing is to talk about it and challenge sometimes illogical established behaviours. Always ask why. I've been so uplifted by the responses and progress we have made by simply starting a conversation. Sustainability requires collaboration, not a top-down approach.

Any further acknowledgements?

I'd like to recognise Sarah Peters (a student peer) and Dr Ruchi Baxi (deputy director of public health) as core members of the student-faculty collaboration. In addition, Dr SanYuMay Tun, an expert in ESH, generously facilitated the workshops and has now taken on a consultancy role at the medical school until a newly funded position is filled.

Osler House News

Thomas Brockwell
(2016 Oriel College), President, William Osler House

I write this as the last of the hot cross buns goes stale. Much like Easter, the reopening of Osler House has proved a somewhat movable feast! Our long-running campaign is set to emerge victorious with our home to be reclaimed by the end of July.

With sport back on the agenda, the myosin heads of Oxford's clinical medics have been crossbridge cycling at rates not seen since pre-pandemic days. Buoyed by increasing financial support from alumni, the Boat Club's two women's crews and the mixed 'beer boat' are determined to storm Summer Eights in June and get us back on the bumps charts for the first time since 2016.

In rare defiance of the oars-based sporting hegemony under the dreaming spires, our Sports Reps threw down the (virtual) gauntlet at the feet of our friends in the Fens who thrusted back with a dual pronged challenge for the most miles run and cycled over a fortnight. Thus, the stage was set for the inaugural StraVarsity. Roused by a background of (online) cries of "bleed dark blue" and "where's your vaccine?", the might of Osler House routed the Tabs with 1,749 miles run and 1,713 miles cycled to 940 and 1,383 miles respectively. Thorough readers of the Alumni magazine may note the serendipitous overlap of the StraVarsity fortnight with Tingewick's 48-hour run; a victory of brains over brawn perhaps?

> *"...the complete removal of FY1 ranking credits from publications and extra degrees took all the UK's medical students completely by surprise. The resistance was soon launched...*

Leaving sport behind, it falls upon me to flag the deterioration of relations between students and the UK Foundation Programme Office. After last year's Situational Judgement Test debacle, tensions were already running high. Cue the UKFPO turning to the ex-US-President-who-shall-not-be-named for administrative inspiration and taking to Twitter to issue policy declarations. Thus, the complete removal of FY1 ranking credits for publications and extra degrees took all of the UK's medical students completely by surprise. The resistance was soon launched with the rise of National Med Soc as the co-ordinating body, and the past six months has seen 6,516 people sign the petition against the changes, and Med Soc after Med Soc declare 'no confidence' in the UKFPO. Expect a Bolshevik/ Menshevik split in National Med Soc followed swiftly by the storming of the Winter Palace (address: UKFPO Office, Birmingham) by the time the next newsletter lands...

Returning to the land of positivity, our Development Officer, Sarah, has been at the heart of the effort to haul Oxford Medicine out of the smog-filled 20th Century into a brighter, greener future. Her Green Impact Scheme has already seen the modernisation of the first-year Medical Sociology course and a reduction of waste in the Clinical Skills Lab. With overwhelming support from the Clinical School leadership, we're excited to see what more we can do to improve care for our planet.

Now for the moment we've all been waiting for: we have two marvellous celebrations of freedom in the diary for the summer. In July, we're waving off our latest crop of doctors with a ball held at the Greek Revival church-now-bar Freud. The night is set to feature wood-fired pizza, plenty of bubbly, a fair few worse for wear finalists, and a return of the headliners 'Fleetwood Macrophage'! Then in August, we're opening the doors of Osler House for the first event on home turf since February 2020; throwing caution to the wind regarding the British weather, we'll be hosting the annual Garden Party as Entz look set to drain their budget on Thai curries, giant chess, a funk band and of course a bop at the end.

Tingewick Hall, usually the scene of pantomimes and bops, badminton, orchestras and OSCEs..... became an unlikely barometer of the story unfolding in the main hospital building.

Medical School News: A testament to an unlikely ally

Dr Catherine Swales
(1997 Wadham College), Director of Clinical Studies, Oxford

I'm not sure I should use a politically-partisan opening gambit, but Obama's notion of "The audacity of hope" is, I believe, where we find ourselves now. The deluge has eased, and the tide is beginning to turn. The change is slow and careful, with restrictions still in place and so many losses still felt - but within the incremental return, distinct moments emerge that seem to mark the beginning of the end. On the face of it and at the time, each seems a purely administrative event: logistical and task-orientated and therefore not immediately profound or poetic ...but with hindsight one can say: "That was it". The sudden drop in student roles advertised by NHS Professionals, the military finally moving out of the John Radcliffe, and the return of Tingewick Hall all took their place in the story. The latter may sound trivial, but in truth, it was far from it. Tingewick Hall, usually the scene of pantomimes and bops, badminton, orchestras and innumerable OSCEs, was loaned by the School to the Trust during the crisis - and it became an unlikely barometer of the story unfolding in the main hospital building. Used to store PPE and spare ITU equipment, its capacity was a measure of the clinical need: the worse the crisis, the emptier it was - only to be immediately filled again as more equipment was delivered to shore up the tide. Finally it filled for a different reason: as the patients recovered, clinical areas began to shed the extra kit. The number of beds and pumps, monitors, ventilators and drip-stands, gowns, gloves and goggles all rose and fell over time; but finally the storage need continued to rise until it was clear the worst was over, and it was emptied altogether, cleaned and returned to us in time for Finals. That simple Hall evokes so many memories in so many students and staff, but this new and unexpected one was very moving indeed. I visited it with Trust estates the morning it was cleared for the last time. Squeezed in amongst the equipment that had supported so many patients, students and staff was an extraordinary moment, and we all (burly removal men included) stared and shared a moment of silence at what had passed. Even the toughest of us had tears in our eyes. Sometimes the strangest places have the deepest resonance: thank you Tingewick Hall.

And so the audacity of hope continues. Placements that had suffered the most are back on track, bedside teaching has been resurrected and the Finalists have made their way through covid-contingent exams. If Tingewick Hall was the infrastructure sign of new things, Finals was the human face of it. Delivering half the clinical exam online, with the 'talking stations' being remote was a mammoth task for Divisional Learning Technology and all our faculty and admin. The latter undoubtedly deserve the greatest round of applause, simultaneously running eight Teams-based carousels, each with 10 breakout rooms, every one staffed by two administrators, four examiners, two actors and four students – six times per day. Oversight and "mission control" was based at Eagle House: with multiple screens it looked more like London Heathrow than a teaching environment, but it was extraordinary. When one candidate vanished mid-station, they were phoned, reassured and assigned a new carousel, all within two minutes of their internet dropping out. I wouldn't have wished it on them, but they did brilliantly - and sometimes something needs to go wrong for you to know that you can make it right.

For other years, their eyes are fixed on exams, which are new in some way for both cohorts. A new summative MCQ looms for year four, and synoptic inter-disciplinary exams for year five. A big ask, but a huge step forward – and despite disruption and upheaval they will do great. Everything I see and hear shows me just how much they know - and can apply. Even now, the crucial clinical reasoning skills are there; they don't just recall, they think. Humbling after all that they've all been through.

And so as I started with a hall, I end with a building – or the audacity to hope for one. The Medical Sciences Division have commissioned architects to understand the scope, scale and design of a potential new Medical Education and Training Centre at Oxford; an institute to that hopes to draw all elements of learning under one roof – undergraduate, postgraduate and research training each having their input and influence. Very early days, and very aspirational – the vision is for a Centre that is first in kind, anywhere in the world – but even if it hits the buffers, for me to spend time planning and hoping with those who put students and learning front and centre of everything that they do is extraordinary. A shared psychological phoenix from weary ashes.

And finally from Obama to Gorman. Her astonishing poem at Biden's inauguration spoke to something much grander and more profound - but the point of poetry is that the reader brings their own subtext. And so I quote her on behalf of us all:

"When day comes, we ask ourselves where can we find light in this never-ending shade?

The loss we carry, a sea we must wade. We've braved the belly of the beast"

As she says: the dawn is ours before we knew it. 'Til next term, adieu!

Dr John Reynolds (1975 St Catz), Associate Head of Medical Sciences Division (Clinical Affairs) and Consultant Physician and Clinical Pharmacologist, John Radcliffe Hospital, Oxford

"Just four miles from level seven at the JR, the Otmoor RSPB reserve has been one of the places I gravitate to for a quiet hour or so at either end of the day whenever I can. It is a remarkable place with an abundance of wildlife where I can indulge my hobby of wildlife photography and let the bustle of the day job quietly subside".

Designed by Jess Aumonier