Oxford Medicine

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Winter 2023



Malaria Vaccine Prof Sir Adrian Hill Sleep Regulation Dr Lukas Krone

AI in Healthcare Drs Scarlett Harris & Lily Watson Suicide in Doctors Prof Keith Hawton And much much more...

Cover image by Dr Kristoffer D. Fehér. "Orchestration of sleep" created with makeahuman 1.2.0 and adobe photoshop 25.2

The New School of Medicine and **Biomedical Sciences:** What, How and Why?

Catherine Swales, Director of Clinical Studies David McCartney, Director of Graduate Entry Medicine Robert Wilkins, Director of Preclinical Studies and Biomedical Sciences

This edition of Oxford Medicine provides an opportunity for us to update you on recent activity in the medical school. Historically, the official administrative home for the medical school was within the Medical Sciences Divisional Office but changes in culture, governance and compliance meant the School needed to become more operationally independent and break out on its own. On 1 August 2023, the preclinical, clinical, graduate entry and biomedical sciences courses were formally brought together as a completely new academic entity within the University, creating the School of Medicine and Biomedical Sciences. The formalisation of the combined School, and its union with Biomedical Sciences, represents a hugely significant and exciting step forward for medical/biomedical sciences education and all our students and staff, plus the opportunity to build on work already started. So why might we need to work more closely together? The good reasons range from improving student experience, both educationally and a sense of 'belonging', to economy of shared endeavour and operational oversight (which sounds a bit dull and dry but is becoming ever more important, not least to the GMC).

The most important drivers were our students. Those on the six-year A100 medical programme now stay in Oxford for the whole of their degree. In the past there was traffic principally between Oxford, Cambridge and London after preclinical, but this has now fallen away to leave opportunities for greater linkage and collaboration between the preclinical and clinical courses. In addition, students studying Biomedical Sciences (which replaced Physiological Sciences in 2010 and recently became a 4-year course) share many common lectures with the early-years pre-clinical students. This close relationship, with threaded content such as Epidemiology, Public Health

and integrated clinical anatomy, throughout all years of the medical programmes, leaves open the possibility of shared opportunities. The covid pandemic shone a spotlight on issues that we had no idea existed. For example, when students had to report their positive covid tests to the University the form asked them to pick their academic department but there wasn't one listed for the medics and BMS students. It sounds trivial but it was far from it; at a time when they felt most isolated and at distance they had no "home". Above all things, that needed to change.

University education, with its demands and responsibilities, is changing at a dizzying rate (revolution more than evolution in many places) and consequently the academic delivery and administration of our courses has become more complex with higher stakes. For teams who work on elements of the four programmes to be able to share, collaborate and support each other creates a new and exciting sense of combined purpose and strategy for everyone across these incredible courses. It will also provide a bedrock for the looming expansion of medical student numbers (deep breath, and something for another edition!).

That said, the cultural baby that is Oxford Medical School is not being thrown out with the operational bathwater. Some things may have changed, but the new School will maintain and defend the core values and experiences that we hope that you will all remember from your time in Oxford: a strong emphasis on the academic and scientific basis of medicine, inspiring teaching from world-renowned scientists and academics, and a rich and supportive clinical experience. And somewhere that was, and ever will be, your home.

** The most important drivers were our students

President's Piece



Dr Lyn Williamson (St Anne's College, 1974) OMA President

Enjoy this smorgasbord of mini-masterpieces and little gems - contributions from Oxford Medical alumni reaching across the arch of time - from the wise reflections of our oldest alumni to fearless predictions of the youngest.

Shout it from the rooftops - Adrian Hill's long campaign for a malaria vaccine is (almost) won. Recommended for widespread use in infants in Africa, it brings an exciting new chapter of hope for millions of children worldwide.

Lukas Krone introduces us to the emerging science of mechanisms of sleep regulation. Sue Burge enthusiastically entices us into the Oxford Physic Garden. Scarlett Harris and Lily Watson review AI in healthcare and warn physicians to keep control, whilst Kate McGibbon bemoans the comic contradiction of the NHS introducing AI before full digitisation.

Keith Hawton kindly accepted our invitation to help us make sense of suicide in doctors and we are grateful for his wise words. Ginney Saxton reminds us that, even in this technological era, simple acts of kindness to trainees will pay forward for future generations of doctors.

Rita has been a constant from the dawn of the clinical school in 1939, but her form has changed. Paul Morrish investigates. Look carefully at the pictures and you might see a bit or even all of yourself.

F1 doctors Leasha John. Elizabeth Hatton. and Jack White, share both their predictions for future treatments and their resilience strategies. Meanwhile medical students Jewel Bennett (Osler House) and Tolu Duckworth (Tingewick) bubble over with energy and enthusiasm.

As the links between OMA, and the new school of medicine and biomedical sciences strengthen, it is timely to examine the shoulders of the giants on whom the school was built. Read about Dennis Noble, from the preclinical school, and of the Directors of Clinical Studies in the centrefold feature by Rosie Fitzherbert Jones. Each of them brought something special to the medical school, but we give the final word to the late Professor John Ledingham, one of our finest clinical teachers: 'In Oxford the emphasis is on you thinking for yourself.'

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Malaria – Approaching the Endgame?



Professor Sir Adrian V. S. Hill KBE FRS FMedSci FRCP (Magdalen College, 1978) Director of the Jenner Institute, Lakshmi Mittal and Family Professor of Vaccinology at the University of Oxford, honorary Consultant Physician in Infectious Diseases, and Fellow of Magdalen College, Oxford

At lunchtime on 2nd October this year about 20 people, including a television documentary crew, were packed into my one-person office at the Jenner Institute in Oxford - to listen to a press conference. This was led by the Director General of the World Health Organisation, Dr Tedros Ghebreyesus, who was announcing a decision on a malaria vaccine. This was the exciting R21/Matrix-M that has been worked on in Oxford and elsewhere for the last ten years. Made by my graduate student, Kath Collins, in 2011, no-one knew what the WHO had decided. On a large screen, watching too, were the lead investigators from five trials sites in Africa who are still running follow-up in the key vaccine licensure trial that enrolled 4800 young children two years ago. And the Serum Institute of India, our amazing large-scale manufacturer and commercial partner in Pune, were on tenterhooks too. I had thought all these key announcements would have been shared with the company and trialists first but not in this case.

Dr Tedros came right to the point. There was good news on malaria vaccine licensure. The R21 vaccine was to be recommended for widespread use in Africa with an expanded age range from 5-36 months based on the extensive R21 safety and efficacy data that the WHO policy advisory group had reviewed. Cue gasps, hugs, even tears, followed by cheers - online and across four continents. Yes, four, as our vaccine adjuvant is from the US company Novavax.

Malaria control has needed a lift. Much progress was made from 2000 to 2017 with almost a halving of the million malaria deaths in 2000 over that period, but deaths are now higher again at 620,000 a year. And that has happened despite over \$4 billion being spent annually deploying a range of interventions, from bed nets and insecticides to rapid early treatment and chemoprevention. Vaccines now offer a new intervention that, at least with R21/Matrix-M and its higher efficacy of about 75%, could well prove to be the most impactful tool yet.

But vaccine success has come slowly in malaria. The first studies were in 1908, the first human trial in the 1940s. Since then, over 140 vaccine candidates reached clinical testing with only a handful looking at all promising. It's a welcome change to explain success having spent years explaining why it has been so difficult. Our R21 vaccine induces unusually high antibody titres against a very conserved region of the coat protein of sporozoites. This is a repeat of just four amino acids, NANP over 20 times, so that in principle the parasite would have to mutate all twenty to escape the vaccine induced immune response. The big challenge has been both reaching the protective level of antibodies and then maintaining it. To do so we used a new nanoparticle that comprises hepatitis B antigen internally, to allow nanoparticle assembly, and a full coating of the malaria sporozoite antigen on the vaccine surface (Figure 1). With a saponin-based adjuvant, the Matrix-M, we saw exceptional immunogenicity and efficacy in the first six months of pre-clinical testing.



Figure 1 :Depiction of the R21 and RTS,S malaria vaccine immunogens. The surface of R21 (made in 2011) is coated with the circumsporozoite protein of Plasmodium falciparum which has a highly conserved central NANP repeat. This antigen is fused to the N-terminus of the hepatitis B surface antigen (HBsAg) to allow assembly of the nanoparticle which happens spontaneously in vivo and also in the yeast strain used for biomanufacturing. The surface of RTS,S, made in the late 1980s, is mainly HBsAg: it was not possible to express the fusion protein alone to generate a nanoparticle fully coated with malaria antigen at that time. The higher proportion of malaria antigen in R21 also allows a lower vaccine dose (5µg rather than 25µg) to be used, increasing yield of manufactured doses and reducing the cost per dose.

Ref: Collins KA, et al. Enhancing protective immunity to malaria with a highly immunogenic virus-like particle vaccine. Scientific Reports. 2017;7:46621

The R21 vaccine was designed to be an improvement on the then leading vaccine candidate in 2010, RTS,S/AS01 or "Mosquirix" from GSK. For R21 we increased the proportion of the malaria antigen and used less of the hepatitis B. GSK are now also planning their first large scale deployments next year in African children after their WHO approvals. But that vaccine, designed in the mid-1980s, has had a very bumpy road with modest efficacy and many pauses, notably for safety signals in the phase III licensure trial that required a million child vaccine "pilot implementation" program to confirm adequate safety and allow regulatory approvals. However, the scale of manufacturing of RTS,S is still very limited with only about 6 million doses available next year for over 40 million African children.

In contrast, the Serum Institute of India, who were by far the largest manufacture of the "Oxford-AstraZeneca Covid-19 vaccine, expect to be able to provide well over a 100 million doses of R21/matrix-M next year, and more as required. UNICEF have already made a huge order, perhaps encouraged by the much lower price of R21/Matrix-M (<\$4 per dose) than RTS,S. This should allow widespread deployment of the R21 vaccine which has the significantly higher efficacy of 75%, first identified as an efficacy goal for malaria vaccine developers by WHO back in 2013. If R21 can be deployed as expected it should save hundreds of thousands of lives a year in Africa alone.



Figure 2. A child being immunised with R21/Matrix-M vaccine at Nanoro, Burkina Faso (courtesy Mehreen Datoo).



But there is still more to do in malaria vaccines and a lot is happening. Simon Draper's group in the Biochemistry department has a blood-stage vaccine in African trials that could be combined with R21. Sumi Biswas, at the Jenner Institute, has two very promising transmission-blocking vaccines in clinical development. So, a multi-component multistage malaria vaccine is on the horizon and that could lead to an acceleration of the numbers of countries being declared malaria free, aiming for eradication perhaps in the next 15 years.

However, that will require a vaccine against Plasmodium vivax as well as Plasmodium falciparum. P. vivax has been very neglected by vaccinologists but is now being targeted anew with vaccine approaches shown to work well for Plasmodium falciparum. And, of course, the excitement about mRNA vaccines for Covid has not been lost on the malaria field. But the realists appreciate that it was much easier (and quicker!) to make Covid than malaria vaccines.

After 20 years of undertaking phase I and II early-stage vaccine trials, with far more disappointments than successes, being part of two successful phase 3 licensure trials in three years has been unexpected, exhilarating and ... exhausting. Many have moaned, justifiably, that if all vaccines could only be developed at the pace seen in Covid-19 we would have many more useful vaccines much more quickly. That is undoubtedly true. But doing this in an academic setting – even with the extraordinary individuals and teams that come together for these major trials – is often overwhelming and persistently intense. I am beginning to understand why big pharma has thousands of staff deployed on such licensure trials, and a little of what they may all be doing.

References

- 1. Collins, K. et al. Enhancing protective immunity to malaria with a highly immunogenic virus-like particle vaccine 2017 Scientific Reports 7: 46621
- 2. Datoo, M. et al. 2021 Efficacy of a low-dose candidate malaria vaccine, R21 in adjuvant Matrix-M, with seasonal administration to children in Burkina Faso: a randomised controlled trial. Lancet 397: 1809-1818
 - Datoo, M. et al. 2022 Efficacy and immunogenicity of R21/ Matrix-M vaccine against clinical malaria after 2 years' follow-up in children in Burkina Faso: a phase ½b randomised controlled trial. Lancet Infectious Diseases 22:1728-1736.
 - Datoo, M et al. 2023 A phase III randomised controlled trial evaluating the malaria vaccine 1 candidate R21/Matrix-M™ in African children. Lancet In Press. (Pre-print at https://papers.ssrn. com/sol3/papers.cfm?abstract_ id=4584076).

Switch, clock and hourglass – elucidating the mechanisms of sleep regulation to advance sleep medicine



Lukas B Krone, Dr. med., MSc & DPhil in Neuroscience (Oxon) (Merton College, 2016) Sir Henry Wellcome Fellow. Sleep Neuroscientist and Clinical Somnologist. He hopes to advance our understanding of the regulation and functions of sleep and aspires to become an astronaut.

Sleep is a vital physiological process. Like eating or breathing, sleep is tightly controlled. Yet unlike nutrient or blood gas sensing, which ensure that essential metabolic parameters stay in balance, the principles governing the regulation of sleep have remained elusive until today.

The Viennese neurologist von Economo started the search for the brain regions that control sleep and wakefulness with his 1930 paper, "Sleep as a problem of localization" (1) describing how viral lesions in encephalitis lethargica located in the hypothalamus or 'interbrain' might cause insomnia or somnolence. Careful clinical observation led him to conclude that centres for sleep and wakefulness are localised in the brain, antagonising contemporaries who believed that sleep was regulated by peripheral mechanisms such as asphyxiation by carbon dioxide, hypnotoxins in the blood and cerebrospinal fluid, or vasomotor mechanisms causing anaemia of the brain. His observations began the search for the circuitry underlying sleepwake control, the foundation for the later conceptualisation of a 'sleep switch'.

The sleep switch

A flip-flop switch became a guiding principle of sleep research (2) following the demonstration of sleep-promoting properties of the preoptic hypothalamic region (3), wake-promoting properties of the ascending reticular activating system (4), and the delineation of their projections. This concept explains the rapid and complete transition between vigilance and sleep and the coordination of sleep- and wake-associated functions. With the discovery of more nuclei that induce transition between sleep and wakefulness, and between rapid eye movement (REM) and non-REM (NREM) sleep, the concept was expanded by another switch regulating transition between these two sleep states (5). However, while the sleep switch model helps describe the interaction between certain nuclei, it does not explain why and when the brain changes its vigilance state.

The circadian clock and the homeostatic hourglass

Timing, duration and intensity of sleep are regulated by two interacting mechanisms, a circadian and a homeostatic process (6). The circadian process describes the fluctuation of wake propensity and other physiological functions in a 24-hour rhythm. The molecular principles of this clock mechanism are well understood and the 2017 Nobel Prize in Physiology and Medicine was awarded for research in this field. The neuroanatomical 'seat' of this clock is also known. The suprachiasmatic nucleus of the hypothalamus is the central pacemaker, driving biological clocks that exist in most cell types of the body (7). However, individuals can detach their sleep timing from the 24-hour rhythm, by getting up early or skipping one or more nights of sleep, and so to prevent damage to brain and body a homeostatic mechanism is needed. This hourglass process is a core mechanism, keeping track of accumulating sleep debt during wakefulness and adjusting subsequent sleep accordingly, but its molecular and anatomical correlates have been unknown.

Regulation of sleep homeostasis by the cerebral cortex

The canonical view was that the nuclei constituting the sleep switch in the brainstem and hypothalamus sense and integrate signals of sleep homeostasis, but conclusive evidence was lacking. In contrast, the cerebral cortex has never been considered as part of the sleep-wake regulatory circuitry despite properties that relate it to the signalling of sleep debt. For example, the cortex generates 'slow waves' on EEG, the hallmark of sleep, and these slow waves are regulated in a local



Figure 1: Silencing a subset of cortical neurons increases wake time and reduces the homeostatic response to sleep deprivation in mice Left: silenced pyramidal neurons in neocortical layer 5. Middle: three-hour difference in total sleep time per 24 hours between control mice and conditional knockout mice with a subpopulation of silenced cortical neurons. Right: Difference in sleep intensity, measured as slow wave activity relative to baseline, between control and conditional knockout mice. For more details see Krone et al., Nature Neuroscience (2021).

and use-dependent fashion. Areas used most intensely during wakefulness show elevated slow waves during subsequent sleep (8). After an extended period of wakefulness, slow waves can even occur while an individual is still awake, leading to errors in task performance (9). This suggests that cortical areas can selectively 'switch off' during wakefulness when a sleep debt has accumulated. Yet the possibility that the cortex contributes to sleep regulation was never tested. My DPhil project aimed



Figure 2: Switch, clock, and hourglass – the brain's tools for sleep regulation Top: The state of the sleep switch determines if an individual is awake or asleep. Middle: The circadian clock controls the rhythmic variation of wake propensity oscillating in a 24-hour rhythm. Bottom: The homeostatic process reflects the sleep debt, which accumulates during wakefulness and dissipates during sleep. For an up-to-date overview of the two-process (circadian and homeostatic) model of sleep regulation see: Borbély, Journal of Sleep Research (2022).

to clarify if manipulation of cortical activity can modulate sleep homeostasis. In a set of mouse experiments, published in *Nature Neuroscience*, we demonstrated that silencing a subset of cortical neurons affects cortical regulation of slow waves and reduces the daily amount of sleep by about 3 hours (10). Furthermore, we found that build-up of slow waves with wake duration was reduced in mice with silenced cortical neurons, suggesting that the cortex determines the function of the hourglass. Putting the cerebral cortex on the map of the sleepregulating circuitry opens a new field of sleep research.

Cortical manipulations to improve sleep

The involvement of the cortex renders it an ideal target to manipulate sleep. Elevating or mimicking the homeostatic sleep drive could help falling asleep or maintaining sleep. In contrast, lowering sleep debt or masking its effects on performance would be beneficial in situations requiring sustained attention. The molecular underpinnings of sleep debt have recently been investigated. Change in chloride concentration within the cortical cells whose chronic silencing slows the hourglass process, mirrors the level of sleep debt (11) and cortical infusion of drugs that raise or lower intracellular chloride concentrations appear to induce or recover local sleep debt. In addition, a different set of cortical neurons may trigger nesting and sleep initiation in mice through two pathways that project to different elements of the sleep switch (12). An alternative approach to manipulate cortical activity is to use 'electroceuticals'. Noninvasive brain stimulation exerts its effects on brain networks and behaviour by exciting or inhibiting cortical areas and has been used to influence sleep-wake patterns, sleep-related brain oscillations, and memory consolidation during sleep in healthy volunteers. However, attempts to facilitate sleep initiation and boost the amount or quality of sleep in insomnia patients have



Figure 3: The circadian clock and the homeostatic hourglass interact with wake-promoting stimuli in determining the state of the sleep switch. The central circadian pacemaker pushes the sleep switch towards the wake- or sleep-state depending on the time of the 24hour day. Distributed hourglasses representing the homeostatic process push the sleep switch towards the sleep-state when sleep debt has accumulated. In contrast, psychologica and physiological stimuli can keep the sleep switch in the wake position. Figure concept: Dr Lukas B Krone. Figure design: Dr Kristoffer D Fehér.

** The best strategy to induce physiological sleep remains to elevate sleep pressure through sleep restriction.

not been successful (13). Understanding the molecular, cellular and circuitry of cortical sleep regulation remains critical to successfully target the cortex to improve sleep.

The need for neuroscience-based sleep medicine

Sleep restriction is a key element of cognitive behavioural therapy for insomnia (CBT-I) but only about half of the patients receiving CBT-I achieve full remission (14). For long-term treatment of insomnia, the harms associated with prescribed substances outweigh the benefits (15). While some drugs help establish a stable circadian rhythm, none accelerate the homeostatic process that would initiate physiological sleep and its associated functions like memory consolidation; it remains essential to establish the neuronal mechanisms through which the cerebral cortex modulates sleep. von Economo wrote that "the exact knowledge of the localization of the center for sleep regulation ... would make it possible to treat insomnia and other sleep disturbances in a better and more active way than by drugs or by the roundabout way of hydrotherapy and psychotherapy." (1) We are now entering an era of neuroscience-based sleep medicine in which the delineation of mechanisms underlying sleep homeostasis will pave the way for improved treatment.

Acknowledgements

I extend my heartfelt thanks to Dr. Kristoffer Fehér for creating the captivating cover image and brain illustration. I would also like to express my gratitude to Jack Hamilton for proofreading and language editing this article. Special appreciation goes to my DPhil supervisors, Prof. Zoltán Molnár and Prof. Vladyslav Vyazovskiy, as well as my academic great-grandfather, Prof. Alexander Borbély, for their insightful comments on the manuscript.

Bibliography

- 1. C. V Economo. J. Nerv. Ment. Dis. 71, 249–259 (1930).
- C. B. Saper, T. C. Chou, T. E. Scammell. *Trends Neurosci.* 24, 726–731 (2001).
- 3. W. J. H. Nauta. J. Neurophysiol. 9, 285–316 (1946).
- 4. G. Moruzzi, H. W. Magoun. *Electroencephalogr. Clin. Neurophysiol.* **1**, 455–473 (1949).
- 5. J. Lu et al. Nature **441**, 589–594 (2006).
- 6. A. A. Borbély. Hum. Neurobiol. 1, 195–204 (1982).
- C. Dibner, U. Schibler, U. Albrecht. Annu. Rev. Physiol. 72, 517–549 (2010).
- 8. R. Huber et al. Nature **430**, 78–81 (2004).
- 9. V. V. Vyazovskiy et al. Nature **472**, 443–7 (2011).
- 10. L. B. Krone et al. Nat. Neurosci. 24, 1210–1215 (2021).
- 11. H. Alfonsa et al. Nat. Neurosci. 26, 64–78 (2023).
- 12. K. Tossell et al. Nat. Neurosci. 26, 1805–1819 (2023).
- 13. L. B. Krone *et al. J. Sleep Res.* **n/a**, e13927 (2023).
- 14. C. M. Morin *et al. JAMA* **301**, 2005–2015 (2009).
- 15. F. De Crescenzo *et al. Lancet* **400**, 170–184 (2022).

AI and the Future of Healthcare



Scarlett Harris (Magdalen, 2013) Recently graduated from Oxford, having squeezed a DPhil in the middle. Academic Foundation Trainee, St Mary's Paddington

Lily Watson (Jesus College, 2016) Academic Foundation Trainee, Bristol (with input from the Meakins-McClaran medallists)

Introduction

2023 was the year artificial intelligence (AI) rooted itself firmly at the forefront of the public consciousness. Defined as the ability of a machine to perform cognitive functions typically associated with human intelligence, the concept of AI was first documented by Alan Turing in his 1950 paper *Computing Machinery and Intelligence*. Five years later, the programme Logic Theorist was developed and capable of performing automated reasoning, seen by most as the first form of AI. Machine learning was pioneered in the 1980s, with computers learning from their mistakes to improve their functionality independent from computer scientist input. The AI industry has subsequently exploded, from generating driverless vehicles, to facilitating multi-omics biomedical research, and assisting radiology reporting. Indeed, the AI-driven world imagined in countless sci-fi novels over the intervening decades may soon be upon us and it will be a major challenge of our time to adapt to this, just as we have done with the arrival of internet in the late-twentieth century. Healthcare is no exception and there are potentially great benefits, as well as significant harms, with the introduction of AI. In this article we discuss the possible impacts of AI on the doctor's journey, from applying to medical school to a career as a consultant, highlighting key questions which we hope the medical community will be able to answer in the coming years.

First steps: Applying for medical school

Today's children are likely to grow up in a world where AI is commonplace, with their education being no exception. One would hope for a world where AI technologies aid learning significantly: tailoring explanations to each student, analysing areas of weakness for development and making lessons more interactive. AI may even help quide their career choices. After all, who could know you better than the technology you carry on you every day, capable of analysing every tweet and google search? However, there is significant risk that those without access to the latest technology could lose out in the competition for medical school entry. The pandemic has taught us that the distribution of technology is far from equitable; this may prove particularly damaging in medicine, where we are striving for a diverse range of candidates to represent all communities. On the other hand, all medical school interviewers will bring with them a level of unconscious bias which we could remove by using AI to help select candidates. This is, of course, dependent on ensuring that the data on which the AI is trained does not inadvertently introduce further bias into the selection process.

The journey begins: AI at medical school

The impact of AI on education has been a topic of significant debate since the arrival of ChatGPT in late 2022. Capable of providing surprisingly eloquent answers to user-asked questions, this AI Chatbot has already demonstrated itself capable of passing law exams and possibly even the USMLE (United States Medical Licensing Exam), leading to concerns that it may be used by students to write essays or otherwise cheat at exams. On the other hand, some have argued that it can be used to make learning more interactive or as a writing aid to free up student time to focus on content and understanding rather than language construction. Currently, ChatGPT has several limitations which prevent it replacing student work completely; its information is often inaccurate, the references often entirely manufactured, the essays simplistic and its authorship relatively easily detected by examiners or software. However, these flaws may disappear as the model improves and thus there remains the need to determine how we will incorporate ChatGPT and other similar software into medical education.

Furthermore, there will be the need to determine how we incorporate training in the use of AI in medical settings and, perhaps more controversially, which areas of the current syllabus could be jettisoned with AI's arrival. For example, will we see an increasing focus on skills and less on recall of facts as AI replaces the need for memory? Some medical knowledge remains hidden behind journal paywalls and a dependency on AI for up-to-date medical knowledge may inadvertently create exploitative, expensive relationships with journal and software companies which would be particularly damaging in resource poor settings.

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Clinicians need to lead and shape the inevitable introduction of AI into their world.

Establishing oneself: postgraduate training

For many, the early days of doctoring are defined by the initial joy of finally graduating, only to be swiftly crushed by the burden of seemingly endless administrative tasks. These seem to take away from training and patient time but are nonetheless critical for continuity and good patient care. Here, AI may be transformative. For example, one company produces Al software capable of documenting physician-patient interactions in real time. Similarly, it has been suggested that AI may be capable of writing discharge summaries. By inviting Al into the medical record, we can also take full advantage of the information contained within, which is often far too great for a single person to process but can be easily synthesized by AI. Overall, the ideal effect would be to free up physician time for patient-centered tasks and training, and improve care by highlighting key information. However, there are still challenges raised, not least how we keep patient data secure and who is legally responsible for the AI-written medical record.

AI may also generate new training opportunities, particularly when it comes to simulation training. We have already seen advertised virtual reality training for surgeons, allowing for the development of precise surgical skills before operating on real patients. As AI develops further, it is easy to imagine this extending into all branches of medicine, with a range of Al-derived avatars on which to practice everything from our history-taking and communication skills to our emergency management. Conversely, there is the risk that a reliance on AI will lead to a generation of doctors without key skills. For example, companies are producing AI software to analyse radiological images, and their introduction into the clinic may mean future doctors never learn to interpret them. Day to day this is unlikely to be an issue and will allow more rapid care, but what if doctors are no longer skilled enough to confirm the AI result is accurate yet remain legally liable in case of an AIderived mistake.

An end and a beginning: life as a consultant The road to consultant-hood is long and variable, and the



medical world into which we take our first tentative steps may be transformed completely by the time we end our training, and even more so when we end our career. Al will undoubtedly make some aspects of this new world incredibly exciting. For those wanting to pursue research, Al offers an unprecedented ability to process and analyse data. We may find new fields develop as the amount of available data increases, just as old ones close. For example, will future pathologists spend more time at their microscope or interpreting the AI-produced sequencing reports?

Just as our world changes, so too will our patients. Healthcare technologies are already well established, with phones and wristwatches analysing our health. Should we embrace these technologies that aim to empower individuals to take control of their health or are we overmedicalizing a population, increasing health anxiety and physician burden in the process? Is the motivation for developing these technologies profit or beneficial health outcome?

Conclusions

Clinicians need to lead and shape the inevitable introduction of Al into their world. Working with our multidisciplinary teams, politicians, industry and, most importantly, patients we can advocate for technologies which provide maximum benefit for patients and resist those that may be harmful. We propose the following five "rules for Al" which we believe should guide the introduction of Al.

- 1. The doctor-patient relationship must remain at the heart of healthcare.
- 2. Databases on which AI is trained must be representative of the entire population.
- 3. Patients should decide the extent of AI involvement in their individual healthcare and healthcare systems.
- 4. Al introduction into healthcare must align with the principles of evidence-based medicine.
- 5. The physician remains the final arbiter.

Oxford Physic Garden



Dr Sue Burge OBE (St Annes, 1972) Hon Senior Clinical Lecturer in Dermatology. Although retired from clinical practice, continues to teach dermatology. She leads tours at Oxford Botanical Gardens and the Medicinal Garden at the Royal College of Physicians.



Oxford Botanic Garden is the oldest in the UK and recently celebrated its 400th anniversary. It was Oxford's 6th Regius Professor of Physick Thomas Clayton (1575 – 1647) who played a key role in its founding. Clayton studied languages, music and natural philosophy at Balliol College, receiving a master's degree in 1599. After spending several years as Professor of Music at Gresham College in London, he returned to Oxford to complete his medical studies. He became Regius Professor of Physick in 1612, a position he took over from his father-in-law.

Clayton wanted to provide facilities for the study of medicinal plants, but money was needed to establish a physick garden to faciltate this. Henry Danvers, Earl of Danby (1573-1643/4), a distinguished soldier who had retired to live near Oxford came to the rescue. A contemporary account describes that Danvers was "minded to become a benefactor to the University, determined to begin and finish a place whereby learning, especially the faculty of medicine, might be improved". It is also recorded that Danvers "suffered much ill health" in retirement. It seems likely that Danvers would have consulted the eminent physician, Thomas Clayton. One can imagine that Clayton might have raised the need for a physick garden, like those established by universities in Europe in the 1500s, with Danvers. Whatever the impetus, Danvers gave the university £250 to acquire land opposite Magdalen College for a garden. Clayton had a prominent role at the opening ceremony in July 1621 when the Vice-Chancellor laid the foundation stone. Alastair Robb-Smith, the Oxford pathologist and historian, hails Clayton "as one of the greatest, if not the greatest, Regius Professor Oxford has as yet had". We may have no portraits of Clayton but we still have the garden.

The medicinal beds have been reconfigured over the last 18 months to reflect the original purpose of the garden and to strengthen links to Oxford medicine. The new design harks back to the formality of the garden in the 1600s with yew pyramids at the corners of the beds and low lavender hedges (rather than box) dividing larger beds into guarters.

One bed showcases medicinal herbs that would have been used domestically as well as by physicians when the garden was founded. All were listed in the "Pharmacopoeia Londinensis", a pharmacopeia written in Latin and published by the College of Physicians in 1618 for the use of apothecaries and physicians. In 1649 Nicholas Culpepper translated this into English. Culpepper's own "Complete Herbal" published in 1653 revolutionised the practice of domestic medicine which had hitherto generally been the provenance of educated gentlewomen who cultivated herbs and prepared remedies for their households. Such women were excluded from universities but read widely and learnt from other healers, including physicians, with whom some corresponded and even shared medicinal recipes. Herbal lore was passed down orally through the generations and sometimes recorded in family "receipt books". Most herbal treatments may have been no more than placebos, but were surely preferable to the purging, blistering or bleeding employed by many physicians of the time to "balance the humours".

45% of our flowering plants are threatened with extinction. We cannot afford to lose them.

Another bed celebrates the contributions of two 17th century Oxford scholars. The first, Robert Burton (1577-1640), Student of Christ Church, is known for "The Anatomy of Melancholy", published in 1621, the year in which the garden was founded, and one of the most popular books of the 17th century. William Osler said it was "the greatest medical treatise written by a layman". Burton, who suffered from depression himself, recognised the positive impact of physical exercise on mental health. His writing still influences the study of mental illness. The bed includes borage (Herb of Gladness) (Borago officinalis) used for anxiety and melancholy. The second, William Coles (1626–1662), Fellow of New College, published The Art of Simpling (1656) in which he popularised the "Doctrine of Signatures" an ancient belief that plants were "signed by the Creator" so that the shape or colour of the flower, leaf or root, or the place in which the plant grew suggested what illness the plant might treat. Nonsense of course. For instance, the spotty leaves of lungwort (Pulmonaria officinalis) were said to evoke pulmonary miliary tuberculosis, so this plant was used for chest infections. The anthropomorphic root of mandrake (Mandragora officinarum) indicated an extraordinarily powerful plant, and mandrake was used for a variety of ailments, as an aphrodisiac and as a vital component of witches' flying ointments (the antimuscarinic tropane alkaloids in this poisonous plant cause hallucinations, delirium - witches thought they flew- and eventually death). Both grow in this bed.

A midwifery bed features herbs used to help women in labour (or as abortifacients) including mugwort (*Artemisia vulgaris*) "the mother herb", motherwort (*Leonurus cardiaca*), birthwort (*Aristolochia clematitis*) and lady's mantle (*Alchemilla mollis*). Common barley (*Hordeum vulgare*) is host to the parasitic fungus Claviceps purpurea, a source of ergot alkaloids. Bread made from contaminated grain causes blood vessel constriction with gangrene and John Chassar Moir (1900-77), Oxford's first Nuffield Professor of Obstetrics and Gynaecology (1937-67), started investigating the potential of ergot to prevent postpartum haemorrhage in the early 1930s while still working in London. Ergometrine saved the lives of countless women. The Lancet recorded in Chassar Moir's obituary 'It was one of the great medical advances of the 20th century ...'

Treatments such as belladonna, opium, foxglove leaf and colchicine wine were advocated by Sir William Osler (1849-1919), the 21st Regius Professor of Medicine, in his classic



Opium poppy

Lungwort leaf

textbook "The Principles and Practice of Medicine" first published in 1892. A modern medicines bed features these plants and others. The discovery of salicylic acid also has an Oxford connection. Edward Stone (1702–1768), Fellow of Wadham College, publicised the use of willow bark powder for "curing agues and intermitting disorders". Willow (Salix alba) and meadowsweet (Fillependula ulmaria) are sources of salicin from which acetylsalicylic acid (aspirin) is derived and both grow in this bed. Tobacco plants (Nicotiana tabacum) reflect the work of another Oxford Regius Professor of Medicine, Sir Richard Doll (1912–2005) who showed how cigarette smoking led to lung cancer and many other diseases. Genetically modified tobacco plants (Nicotiana benthamiana) are being used to produce a wide range of pharmaceuticals including next-generation antibodies.

Malaria kills more than half a million people every year. In the 1960s Mao Zedong in China ordered a search for new malaria treatments. Tu Youyou, a Chinese chemist with expertise in both modern science and Traditional Chinese Medicine (TCM), found that in 340CE a physician, Ge Hong, had reported that Artemisia annua (Sweet wormwood or qinghao) controlled intermittent fevers. Her team showed that extracts of this plant had antimalarial activity and determined the structure of the active chemical, artemisinin. Tu Youyou received a Nobel Prize in 2015. This story also has an Oxford link. Prof Sir Nicholas White (born 1951) is Professor of Tropical Medicine in Oxford and Professor at Mahidol University in Thailand. White's Thailand team pioneered the use of artemisinin combination therapy, now the first-line treatment for malaria worldwide. By 2006 the WHO was recommending artemisinin-based treatments for malaria. Artemisia annua celebrates both their contributions.

70 - 95 % of people in developing countries depend on traditional medicines. Global health beds will contain plants used in practices such as ayurvedic medicine, TCM and South African 'muthi'. Examples include *Glycyrrhiza glabra* (liquorice) used in ayurveda, Agapanthus africanus used in muthi, Ephedra sinica used in TCM for thousands of years to control coughs (ephedrine, the active chemical, is an effective bronchodilator) and Yaupon, whose leaves contain caffeine, used by Native Americans in cleansing rituals (tea prepared from the leaves was drunk in sufficient quantities to induce vomiting- hence the name *llex vomitoria*). Madagascar periwinkle (*Catharanthus* roseus) was used in many parts of the world to treat diabetes but investigation showed that extracts of the leaves did not alter blood glucose. Instead, the extract caused a profound drop in the white blood cell count. The resulting vinca alkaloids revolutionised the treatment of malignancies such as childhood acute lymphoblastic leukaemia. Many traditional remedies may merely be placebos but as the stories of vinca alkaloids, artemisin and ephedrine show, some traditional medicines warrant further investigation. 45% of our flowering plants are threatened with extinction. We cannot afford to lose them.





Madagascar periwinkle

Suicide in Doctors



Professor Keith Hawton CBE (Balliol College, 1966) Emeritus Professor and Consultant Psychiatrist, Oxford with special interest in epidemiology, factors and prevention of self-harm and suicide. Fellow, Green Templeton College.

Reports of doctors' suicides understandably cause considerable disguiet, not just for family and friends, but also for other members of the profession. They also raise questions, such as: Why did they do it? Surely, they could have got help? And, most pertinently, was there something that could have been done to prevent this sad event? Here are some facts about this issue of suicide in doctors, some thoughts about what can be done to try to help colleagues in distress who may be at risk, sources of help for troubled doctors, and how those affected by the death by suicide of doctors can get support.

Until some years ago, suicide rates in doctors of both sexes in the United Kingdom were elevated above those of comparable groups in the general population. This is in keeping with the pattern in several other countries. However, the rate in male doctors in England has since declined such that their risk has become relatively low. Suicide rates in female doctors in England also appear to have declined to being comparable to those of other women. In terms of numbers of doctors' deaths recorded as suicides in England by the Office for National Statistics, between 2011 and 2021 there were 178 in total - 120 in males and 58 in females, so averaging approximately 11 deaths per year in men and 5 per year in women. This reduction in levels of suicide in doctors is clearly encouraging, but the questions about suicides of individual doctors highlighted above clearly remain, especially as such deaths tend particularly to occur in younger doctors.

What do we know about factors that contribute to doctors' suicides?

To some extent these are similar to influences on suicide in other individuals, including, for example, mental disorders, alcohol and drug misuse, major physical illnesses, disruption of key relationships, and financial problems. But there are other factors somewhat more specific to being a medical practitioner, such as serious adverse outcomes of patient care, difficulties in relationships with clinical colleagues and management organisations, and medico-legal issues, especially those that lead to disciplinary actions. Additional factors that may contribute to risk are knowledge of, and access to, means used for suicidal acts, especially poisoning.

What can be done to prevent suicides of doctors,

and in particular what can colleagues do in this regard? It is important, first, to recognise that we have learned that the prediction of who is likely to die by suicide, whether a doctor or anyone else (including people with mental disorders) is virtually

C What can be done to prevent suicides of doctors?

^{(C} What do we know about factors that contribute to doctors' suicides?

impossible. But a more general approach to helping colleagues who appear to be going through difficult times may be effective. This can include simply reaching out to clearly troubled colleagues, acknowledging that they don't seem to be their usual self, or, if there is clearly a crisis for an individual, offering the opportunity for a friendly confidential chat.

Introducing this possibility with statements such as, 'you seem to be having a difficult time just now; I wonder if you might you find it helpful to have a chat' may encourage a troubled doctor to begin to share their problems. The potential value of someone expressing concern and wish to help in such circumstances should not be underestimated (some the most powerful factors that may prevent suicides are human connection, expression of concern, and showing empathy). Where it becomes clear that a doctor needs help related to mental health or substance misuse problems, in addition to the usual potential avenues for seeking help (e.g., general practice, occupational health, local psychiatric services), NHS Practitioner Health can be a particularly valuable source of help (weblink below).

When a doctor dies by suicide, colleagues may well feel in need of help to cope with the loss.

One easily accessible source of information is *Help is at Hand*, which is available as a pdf and as a free hard copy (link below). Informal discussion with colleagues also affected by the loss may be helpful. In addition, there are several bereavement support organisations in the UK which provide specific help for people bereaved by suicide. Finally, NHS England has recently developed a toolkit for help with the aftermath of suicide by any health professional (link below).

NHS Practitioner Health: https://www.practitionerhealth.nhs.uk

Help is at Hand pdf: http://supportaftersuicide.org.uk/

hard copy: https://www.healthpublications.gov.uk/ViewProduct. html?sp=Shelpisathand2021version

NHS toolkit for health professionals affected by suicide of a colleague: https://www.nhsconfed.org/system/files/2023-03/ NHS-employee-suicide-postvention-toolkit.pdf

It's Caught not Taught



Virginia Saxton (St Annes, 1975) Director of Radiology at The Mercy Hospital for Women. Melbourne

Many of my English colleagues with whom I trained are now retired. So why I am still working? And enjoying it?

My field of Obstetrics and Gynaecology imaging has advanced massively thanks to new high-resolution ultrasound machines, the advent of foetal MRI, advances in genome analysis, all backed up by high quality neonatal intensive care. In addition, thanks to new software platforms I can now teach across the globe (Radiology across Borders https:// ogimagingupdate.wordpress.com). This week I delivered a teaching session to 600 doctors from 72 different countries, helping doctors in the developing world improve their ultrasound interpretations and hence their patients.

But for me it's human interactions, not technical skills, that are key.

A GP friend observed the dearth of caring senior clinicians in the medical workforce. She meant a lack of kind, caring role models for trainees, not disdain for patients, and I agreed.

In Australia it is competitive at every level of medicine. Junior doctors have to work harder, publish more and achieve more to get on. Many find the pressure of constant exams, the relentless expectations, and their fear of failure overwhelming. There is a high rate of burnout (43% for O&G trainees in one UK study (1)) and doctors' suicide remains of great concern. (2). So, we need kinder, more supportive senior clinicians.





As I reflect, many examples come to mind where simple acts of kindness - a well-wishing text to an ill trainee, a listening ear, a bunch of flowers, a card, a prayer-have made important differences both to the recipients, and maybe those observing them. Joy spreads fast around the whole department.

I am a Christian and from time to time I pray with a patient if they wish. A Muslim woman, 10 weeks pregnant, came in with a second bout of torsion. After the scan I offered to pray for her. A week later she returned for a checkup, all was now well, and she said the prayer had given her a lot of peace. A Hindu patient came to us to test her

tubal patency after she had suffered a stillbirth at 36 weeks. "Prayer" she said, "lifted a huge weight off my heart". Another patient I prayed with said to me "don't stop doing this".

Trainees have to learn to deal with difficult colleagues. There are irritating people in our life who are there to 'grow us in grace'. I have found this idea helpful. We are not going to change them however much we try, and their "job" is simply to grow us in grace. One staff member became much less irritating once I realised she was a grace-grower for me. One registrar even promised to "keep growing in grace" after he had left us.... Is active, demonstrative kindness effective? For some trainees I suspect no, but for some it makes a real difference. We can leave a legacy of care and compassion to the coming generations of doctors....if we try.

It's caught, not taught.

- 1. Burnout, well-being and defensive medical practice among obstetricians and gynaecologists in the UK: cross-sectional survey study. Tom Bourne et al BMJ 2019
- 2. A perfect storm: towards reducing the risk of suicide in the medical profession. Ann I McCormack Med J Aust 2018; 209 (9): . || doi: 10.5694/mja18.00221

Kate's Soap Box: AI without Digitisation, a Comical Contradiction



Dr Kate McGibbon (Exeter College, Queen's College, 2012) ACCS Acute Medicine, London

The discussion of artificial intelligence (AI) applications in day-to-day life and work looms large in the media and professional landscape. Medicine is no exception to this repetitive news-cycle-driven affliction, but are we putting the cart before the horse?

There is a comical and irritating contradiction between the struggle for hospitals to fully digitise and the simultaneous explosion of artificial intelligence (AI), an omnipresent buzzword which implies a high-level of digitisation.



Drawing by Dr Chris Mason (Worcester, 1977)

The government plans to meet core digitisation standards, including for 95% of trusts to have electronic patients records by March 2025, with £2 billion invested in secondary care technologies to that end.¹ At the same time the intersection between computer science and statistics, in the form of AI and data science, has evolved to deliver products like ChatGPT which use natural language processing to produce staggeringly fast and comprehensive (albeit not always entirely accurate) answers to queries.

However, a recent survey showed that threequarters of NHS trusts in England, continue to rely on paper.² Even in hospitals that have digitised, the government reports describe substantial variation between organisations and legacy systems which in some cases simply do not work.³ Frustrated healthcare professionals circumnavigate or completely avoid certain features, while medical journals espouse the potential for AI in diagnosis and management of patients.

Pushing boundaries in research advances healthcare but focusing on AI advances, while failing to establish consistent digital tools and learn which tools are required, seems foolish and will restrict the benefits of AI to already successfully digitised hospitals.

My concern is that ignoring this contradiction will lead to greater health inequalities, through digital variation and a hospital postcode lottery. This is contrary to the NHS's purported utilitarian ethics, if the use of QALYs by NICE is anything to go by.

Perhaps I needn't worry, maybe hospitals will devise a direct route to an AI actualised future, bypassing the intermediate technological limitations? We can but dream.

References on request from the author: katemcgibbon1@gmail.com

C Putting the cart before the horse?

F1 Predictions - 2 New Therapies



Dr Leasha John (Oriel College, 2017)

Dr Elizabeth Hatton (St Catherine's College

KarXT for Negative Symptoms in Schizophrenia Dr Leasha John F1 Swindon

For a long time, Schizophrenia medications have largely focused on treating 'positive' symptoms, such as hallucinations, delusions and thought disorder. The 'negative' symptoms, including changes in affect, anhedonia and cognitive disruption, have been neglected with the dopamine-focused anti-psychotic drugs having little impact. However, KarXT is a new drug currently in phase 3 clinical trials showing promise in targeting both symptom groups.

KarXT is an M1/M4 specific muscarinic receptor agonist. M1 is associated with positive cognitive effects, impacting memory, learning and attention, whereas M4 is thought to have primarily antipsychotic effects. Previous attempts to target the muscarinic receptors in schizophrenia have been stopped short because of peripheral procholinergic effects (including gastrointestinal symptoms and syncope). However, KarXT contains trospium, a peripheral muscarinic receptor antagonist, and so these adverse effects have been minimised.

EMERGENT-1 was a 5-week, inpatient, double-blinded study, in which patients with schizophrenia were allocated to KarXT or placebo. Response was quantified by comparing Positive and Negative Syndrome Scale (PANSS) scores pre- and post-treatment. KarXT demonstrated statistically significant improvements compared to placebo across the board in both positive and negative symptoms, as well as improvements in anxiety, depression and uncontrolled hostility. This could signify one of the most significant drug developments in Schizophrenia in decades.

References from author: leasha.john@nhs.net

•• One of the most significant drug developments.

Kaftrio for Cystic Firbrosis Dr Elizabeth Hatton F1 Swindon

A 15th century European proverb states 'woe to the child who tastes salty from a kiss on the brow, for he is cursed and soon will die'. Recognised for centuries, cystic fibrosis is a devastating disease. First described by pathologist Dr Dorothy Anderson in 1938 as a pancreatic disease, it affects exocrine glands, causing severe multi-organ damage associated with significant morbidity

(Oriel College, 2017) F1 Great Western Hospital, Swindon

(St Catherine's College, 2017) F1 Great Western Hospital, Swindon

and premature mortality. The responsible protein defect, CFTR (cystic fibrosis transmembrane conductance regulator) is involved in maintenance of ion concentrations across epithelial tissues and was first identified in the 1980s. Respiratory failure is the major cause of morbidity and mortality, compromised CFTR function resulting in abnormal mucus secretion, recurrent infection, airway obstruction and respiratory function decline. Cystic fibrosis can be severely life-limiting, with patients experiencing loss of autonomy and damage to mental health as their condition dictates their life.

Until recently cystic fibrosis was managed supportively, with an average life expectancy of 37.1 years. Past treatments have included pancreatic enzyme supplementation, antibiotics, mucolytics and lung transplant.

Kaftrio, a modulator therapy that increases processing and delivery of CFTR to the cell surface, is a triple combination therapy containing tezacaftor, ivacaftor and elexacaftor. Made available to UK patients in August 2020, it has revolutionised cystic fibrosis treatment. It is estimated that, when started in adolescence, patient survival is close to that of the general population and the comparative ease of taking the medication has significantly improved patients' quality of life. It is currently available in the UK for patients over 6 years old with F508 mutations, 90% of all patients, and it is hoped that the UK will follow in the footsteps of the US where, as of April 2023, Kaftrio is available to patients as young as 2 years old. By initiating modulator treatment early it is believed eligible patients will avoid respiratory failure, and may live well into old age. What was once a disease of childhood death is no longer, and our practice must adjust.

Although major advances have been made, more work is needed. 10% of patients with cystic fibrosis do not benefit from Kaftrio treatment. Genotypes not targeted by Kaftrio are most prevalent in non-White populations, racial bias continuing to limit treatment. It is critical to identify a universal treatment, and even cure. Research into gene therapy, the introduction of a functional version of the CFTR gene into patient's cells, is ongoing and although progress is slow, encouraging advances have been made. This may provide the way to treat all patients.

References from author: elizabeth.hatton2@nhs.net

what was once a disease of childhood death is no longer, and our practice must adjust.

F1 Survival Page

Painting

Dr Elizabeth Hatton (St Catherine's College, 2017) F1 Great Western Hospital, Swindon

F1 is daunting. It's what you've been working towards for years – every essay, every placement, every exam building up to the day that you can finally call yourself 'doctor'. Of course, there are great things about the job. You're now a key member of the team and



are possibly the face patients see the most. They grow to trust you, and that is truly a privilege. Nonetheless, learning how to separate work from home is essential.

I have always enjoyed art and remember desperately trying to weave this hobby into my personal statement. I talked about my dexterity and my eye for detail, skills I thought were essential for a doctor. However, the escape it provides has ended up being far more important. I rediscovered my love for art during lockdown and have continued through my first months of F1. It helps me switch off at the end of a long day. I particularly enjoy painting portraits and when focussing on the brushstrokes, I leave whatever happened that day behind me.

Climbing

Dr Jack Wilson (Queen's College, 2017) F1 Gloucester Royal Infirmary

I started climbing towards the end of medical school, going to the climbing wall in Brookes because some of my friends went. I really enjoyed the combination of physical challenge and different



techniques, so I started going regularly. As well as being a physical endeavour, the mental part is what makes it so great for switching off from work and other stresses; you can't be thinking about much else when holding on and moving to the next position is stopping you taking a fall! It's a sociable and welcoming sport and helped me make some great friends when moving to a new city to start my foundation training.

I've always loved the outdoors, so a hobby where I spend the day in cool locations in the countryside is a great contrast to my working life; even if I'm only climbing a couple of routes, a day being outside always seems to reset my mental state in such a good way. The other great thing is that there are no fixed training sessions, so it fits around the varying schedule of working in medicine without impacting the level of enjoyment I take from it.

Crocheting

Dr Leasha John (Oriel College, 2017) F1 Great Western Hospital, Swindon

In my spare time I find myself gravitating towards creative outlets. I was a very active sports person but, following an ACL reconstruction this year, my energy is now poured into making clothes by sewing and crocheting. I became enamoured by



both during lockdown (very clichéd) but throughout childhood my mum would always be sewing and so it was always at my fingertips.

I can vouch for it as a stress relieving activity; how can you be thinking if you prescribed the correct PPI when you're obsessively counting crochet stitches or trying so carefully to not pierce your fingers with a sewing machine? My magnum opus thus far was my Magdalen Ball 2023 creation: a full fourpiece ensemble with a top, skirt, corset belt and crocheted shawl to match. I cannot emphasise enough how important it is to have a comfort hobby to wrap yourself in when you just need to reset, like a warm handmade blanket on a rainy day.





ainting by Elizabeth Hattor

Denis Noble



Extracts from an interview for Recollecting Oxford Medicine podcast series with **Professor David Cranston D.Phil** (Wolfson College 1986), Associate Professor of Surgery (Emeritus), Emeritus Fellow Green Templeton on 5 October 2023.

Denis Noble CBE FRS FMedSci MAE is a British physiologist and biologist who held the Burdon Sanderson Chair of cardiovascular physiology at the University of Oxford from 1984 to 2004. He is one of the pioneers of systems biology and developed the first viable mathematical model of the working heart in 1960. He is an Emeritus Fellow of Balliol College Oxford.

As a teenager, he was trained as a Magician by a stage performer, Tommy Dee. He plays classical guitar and sings Occitan troubadour and folk songs (Oxford Trobadors). In addition to English, he has lectured in French and Italian, Japanese and Korean.

Denis Noble was born in 1936 in London to working-class tailors and there is an early photograph of him in 1945 outside their garden in Balham in London, looking so thin after the war as there was so little to eat. He was the oldest of four boys and went to Emanuel School in London and it was here in 1947 that he encountered four brilliant science teachers of whom Harry Hirst in chemistry was the most inspirational.

He secured a place at University College London to do medicine, passed the 1st MB, but then went straight on to a BSc and PhD. So, he never trained clinically but does now have an Honorary FRCP!

Otto Hutter was his PhD supervisor and a mentor throughout his career until his death in 2020. Otto was working on the skeletal muscle and the heart and Denis worked with him on anion transport, but that led Denis to wonder what the cation, potassium, was doing inside the cell. This led to an 'inward rectifier', a channel which switches down when you depolarise the cell, and is an extremely efficient energy saving mechanism, preventing huge leaks of potassium and death. He went on to see if he could calculate the action potential of the heart. This required a knowledge of maths and access to a computer, and while there was a mercury Computer in a Bloomsbury basement the guardians of this machine refused to let him use it as he knew very little mathematics and had no idea what a programme was.

However, he managed to acquire the programming book for the Mercury computer and went to the maths lectures for students, while also working in the lab. After six month of learning integration and programming he persuaded the guardians of the computer to allow him a two-hour slot, from 2-4am in the mornings! His days began at 5am to collect hearts from the slaughterhouse, arriving back at the lab to put them into Tyrode solution. During the day he would dissect out the Purkinje fibres and experiment till 10 o'clock at night. At 11pm he would have a cup of coffee and at 2am went to the computer for two hours. It was a 24-hour rhythm that would go on for three or four days and then he would crash out. A few months later he found the answer and would never forget seeing the first data coming out with the rhythmic up-and-down wave form. The results were written up for a paper in Nature. Denis was 24.

In 1963 he was approached by William Paton, Professor of pharmacology in Oxford, to apply for a fellowship in physiology at Balliol. By this time he had married Susan, a student at Somerville College, who, with Hilary Brown, Dario DiFrancesco and Denis, found that other mechanisms, particularly the HCN¹ channel, were important.

Denis was asked to give an annual review lecture to The Physiological Society based on this work, only to have the subsequent paper rejected by the *Journal of Physiology!* However, it was accepted by *The Philosophical Transactions of the Royal Society* and in 2015, when the society was celebrating 350 years, they chose that paper alongside an extraordinarily distinguished set of previous papers that began with that of Sir Isaac Newton.

It was at this stage in the interview that Denis pointed to his bookcase with 30 facsimile scrolls and 36 volumes of Japanese translation of Chinese medicine kept by the Imperial family in Japan for over 1000 years. He had been the moral tutor to the Empress of Japan when she was a student in Oxford, and this gave him access to this extraordinary archive kept private for over 1000 years. It was a compilation by Tamba Yasuyori in the 10th century of all he had learned of Chinese medicine, filtered by his own Buddhist credentials, excluding toxic metals, and animal products. Japan had turned out to be the guardian of a unique compendium of herbal Chinese medicine.

In 1984 Denis Noble was appointed as the Burdon Sanderson Professor of Cardiovascular Physiology. Burdon Sanderson was the Regis Professor of Medicine in Oxford before William Osler, and was the first person to show the long-lasting nature of the heart action potential showing that the T-wave was the repolarisation wave.

In the 1980's Denis was the founder of 'Save British Science' which resulted from Margaret Thatcher's cut in funding and

Clinician, scientist, magician and Occitan troubadour...be bold!



After retiring in 2004 he worked on *The Music of Life* which was published in 2006. It was a direct challenge to Richard Dawkins, whom he knew well, having examined his thesis in 1966. They met again at a famous debate at The Institute of Art and Ideas festival at Hay-on-Wye which remains available on YouTube and on **Denisnoble.com**.

In the last chapter of *Dance to the Tune of Life* published in 2016, he explores the idea that our knowledge is relative to what we already know, and we ought to recognise what we don't know. He illustrates that with reference to the model of the universe which is exceedingly fragile. His reaction to the Big Bang model (he is a modeller himself and was in discussion with some of the key proponents of this) is that it can't be true and would not predict what we are seeing as some of the earliest structures that are now being accessed by the James Webb telescope.

"There's something missing here, so my feeling about our knowledge of the things that exist, that's the universe, how did they come to exist, the big 'Why' question: why do they exist, the best answer is we don't really know, so I think that a-theism is not a bad description of an agnostic view which I hold."



Asking what he hoped the government would do for science he said:

"I would love to be able to do what I did in 1996, roughly 10 years after Save British Science was formed. I was able to speak with Tony Blair and said: "We have now had 10 years of not being prioritised. Can you look forward to a ten-year period in which you can slowly rebuild that?"

He appreciated that and eventually he appointed David Sainsbury of the Sainsbury family as the Science Minister, who did just that. Hence, we changed the name to 'The Campaign for Science and Engineering.'

When asked if Brexit had damaged science he replied: "Yes, we have damaged ourselves. French colleagues have felt we have thrown away the best science in the European Union, but there is a way back if we only remove this extreme insistence on sovereignty above everything, we could restore some of the damage."

And asking what advice he would give a young scientist today he replied:

"First I would say you will get nowhere unless you get some funding, make a beeline for whatever you can do that will raise funding for yourself, but then try to do what I did for many years: keep 5 - 10% for those barmy ideas which you may not even yourself believe in. You know one of those might be your saviour you never know - be bold!"

¹Hyperpolarization-Activated Cyclic Nucleotide-Gated Ion Channels and Cardiac Function. In the heart, HCN channels control the spontaneous depolarization of the sinus node and, therefore, commands the heart rate.

Directors of Clinical Studies



Rosemary Fitzherbert Jones (St. Hilda's College, 1977) Medical historian and author. Honorary Osler archivist at 13 Norham Gardens for five years. Author of Oxford's Medical Heritage, illustrated biographies of Oxford medical figures over the years.

C the Directors of Clinical Studies have been responsible for the evolution of medical training.

The story of the clinical medical school at Oxford begins in 1939 (there had been one that opened in 1780, but it closed in 1833). Over the years the Directors of Clinical Studies (DCS), have been responsible for the evolution of the medical training as well as the pastoral care of the students.

In the first decades of the twentieth century almost all students doing their preclinical degree at Oxford went to London hospitals to continue their studies. In the 1930s, Sir Hugh Cairns suggested establishing an academic clinical school solely to train doctors to go on to academic posts in the new Nuffield Departments but it did not materialize.

The idea of a clinical school re-emerged when WW2 began. The resultant clinical school was largely due to the work of Dr Alexander Cooke, a physician both erudite and enthusiastic. London medical schools were dispersing students and patients outside London because of fear of bombing in the capital. Dr Cooke felt it was sensible for Oxford students to stay and do their clinical training in Oxford. The school opened within days with sixty students. Dr Cooke was the first DCS, holding the post from 1939-1949 (he was actually called sub-dean, which is the term other medical schools used).

In 1944 the Goodenough Committee on Medical Schools recommended that Oxford should become a small experimental undergraduate clinical school, radically new and ground-breaking. Whilst this caused great excitement, it came to nothing and only five students joined in 1945.

In 1949 Dr Sidney Truelove took over as DCS. He was a gastroenterologist and was famed as an outstanding teacher. If students failed to come up to scratch on a ward round, they were despatched to the library and told to give a presentation the following week.

The student numbers were still low, and Truelove published a memorandum recommending, among other things, better communication between the hospital and the medical school. In

addition, he felt there should be more beds under the control of the professors for the teaching of students.

The problem was addressed by Sir George Pickering who became Regius Professor of Medicine in 1956. He had a lifelong passion for teaching and medical education and, working with his DCSs, was largely responsible for the success of the modern clinical school. Dr John Badenoch became DCS in 1955. He and Pickering travelled round the country, especially to Cambridge (which did not have a clinical school), espousing the virtues of the Oxford clinical school. Subsequent DCSs carried on the good work.

Dr Michael Dunnill, a notable pathologist, who was DCS from 1966 to 1972, remembers telephoning Cambridge tutors and visiting to speak to undergraduates there. Dr Dunnill, as a member of the clinical sub-faculty, produced a memorandum in 1969 proposing changes to the course. These included shortening the clinical course from three to two years. An introductory course was brought in and continuous assessment replaced some of the more formal examinations. Finally a revision course was added in the final three months. This was controversial as it was feared students might be tempted to cruise through the clinical course doing little work but pass finals due to what they learned in the revision course.

Dr Jim Holt took over as DCS in 1972. He worked in the Nuffield Department of Medicine, as a consultant general physician. He was quite junior when he became DCS. He increased the length of the clinical course back to three years and tutored students in the "bridge course" which was set up by Professor Paul Beeson to link the preclinical courses of Oxford, Cambridge or London with the clinical course at Oxford.

Professor John Ledingham served two terms as DCS, from 1977 to 1981 and 1991 to 1995. Well known to us all (and an important founder of the OMA), he was loved by his students and immersed himself in student life. He was always ready to fight the students' battles and he spoke up for them when they



Dr Jim Holt





Sir Christopher Paine

feared losing Osler House, their club and home at the Radcliffe Infirmary, when Green College opened.

He was followed as DCS by consultant radiotherapist, Sir Christopher Paine in 1982. He sent a questionnaire to all the clinical students to learn their views on the course and worked with John Ledingham to improve the curriculum. At this stage the intake was a hundred students. If the number dropped below this, it was financially detrimental to the university.

Surgeon Mr Julian Britton took over in 1985. The reputation of the clinical course by now was such that over three hundred potential students applied for the one hundred and fifty places available. However, he worked with the Nuffield Professors Sir David Weatherall and Sir Peter Morris to interview all the teaching staff to get their views on the course and how it could be improved further. It resulted in the important development whereby general practice became a significant part of the course, with dedicated teaching time.

The baton was passed to radiologist **Dr Basil Shepstone** in 1988. He hailed from South Africa and is fondly remembered as a warm and humorous teacher. One saying was: "Everyone here is clever but you also need to be kind".

Following John Ledingham's second term of office. Professor John Sear became DCS in 1995. He continued his work as anaesthetist and played an important role in the development of Green College and also the Graduate Entry Scheme which enabled graduates with an arts or other degree to enter the clinical school. John Sear selected and taught these students, making sure they learned the necessary basic sciences.

Dermatologist Dr Susan Burge, DCS from 1999-2002 was the first woman in the role. She faced the challenge of two imminent rigorous inspections of the medical school; one by the GMC and one by the Quality Assurance Agency (a body that exists to maintain the standard of higher education in the

Dr Susan Burge





Professor John Sear



Dr Sidney Truelove

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Dr John Badenoch





Mr Julian Britton



Dr Basil Shepstone

UK). The medical school lacked a written curriculum (students were encouraged to explore topics widely as they still are) and final examinations tended to reflect the interests of the clinical examiners, rather than being blueprinted to the curriculum. The clinical teachers collaborated and agreed a curriculum. Examiner training was formalised and examinations were restructured. Sue also worked closely with Stephen Goss, the Director of Preclinical Studies. The medical school passed with flying colours.

The next appointment was **Professor Tim Lancaster** who was DCS for a long tenure (2002 - 2017), the first time the DCS was a GP. He was interested in the academic side of primary care but continued his clinical commitments throughout his time as DCS. He enjoyed hands on teaching and the pastoral care of the students. He is an outstanding teacher and was very much involved in the care of the students. He responded to a request from final year students for guidance regarding their study for finals by developing small group teaching sessions with patients and experts, which evolved into a webinar series. After stepping down as DCS, he spent four years as Dean of Medical Education at King's College London, and is now back in Oxford in clinical practice.

Dr Tim Littlewood took over as interim DCS for a year in 2017. He is a haematologist, with a love of teaching and was nominated as a role model by his junior staff in the BMJ in 2017. The present DCS, appointed in 2018, is rheumatologist Dr **Catherine Swales**. She stresses the importance of team work in the department, from medics to administrative staff. Like previous holders of the post, she relishes the variety of the job, ranging from the pastoral care of individual students, to making major decisions for the future of the medical school.

The result of the work of these fourteen DCSs is a medical school of such excellence that it consistently rates in the top few in the world.





Professor Tim Lancaster Dr Tim Littlewood



Dr Catherine Swales

Poirot, Clues and Psychology



Professor Tony Hope (1970 New College) Emeritus Professor of Medical Ethics, University of Oxford, Emeritus Fellow St Cross College, Honorary Fellow New College

Dr Sally Hope (1975 Jesus College) GP, Woodstock, Oxfordshire (retired) Clinical Assistant Nuffield Orthopaedic Hospital (retired)

'To begin with' Poirot says to his friend, Hastings, 'we apply our psychology. We find three points at which Monsieur Renauld displays a distinct change of view and action - three psychological points therefore.'

This quotation is from the second Poirot novel, *The Murder* on the Links, first published in 1923. Poirot's use of the word psychology here marks the most significant development in Agatha Christie's evolution as a writer of whodunnits.

We first meet Poirot in The Mysterious Affair at Styles (1920). In this novel Poirot is essentially a Belgian Sherlock Holmes. With metaphorical magnifying glass in hand, Poirot inspects the scene of murder in great detail, smelling an almost invisible stain on the carpet, and using a fine pair of forceps to extract a fragment of green cloth. This behaviour demonstrates the brilliance of Poirot but is of little help to the reader in solving the puzzle. In explaining his methods Poirot emphasises the importance of details, and of putting one fact at a time together to form a chain in order to seek a missing link. He makes no mention of psychology.

In this first published novel Christie, unlike Conan Doyle, was attempting to write a genuine whodunnit. It is partially successful. There are clues that can help the reader but by her later standards these are desultory, and the plot depends on some rather arcane pharmacology (that we didn't know despite having been taught by Professor Grahame-Smith).

In The Murder on the Links Poirot (and Christie) undergo a transformation. He is no longer the caterpillar he was in the first novel, but not yet the butterfly he will become. What Christie is beginning to understand is that the physical clues, what might be called sleuth clues, are of little help to readers in solving the puzzle. The 'distinct change of view and action' that Monsieur Reynaud displays, however, can indeed enable the alert reader to solve one of the puzzles in the book.

The term psychology marks Christie's realisation that she must go beyond 'sleuth clues' if she is to set readers difficult puzzles that can be solved. From her very next Poirot novel, The Murder of Roger Ackroyd (1926), Christie developed new types of clue and Poirot never again makes use of a pair of forceps.

Poirot does not elaborate at this stage on what he means by psychology. It includes odd remarks and inconsistencies in what people say, and changes in people's behaviour. But it seems to encompass for both Poirot, and for Christie herself, almost any type of clue other than Holmesian sleuth clues. Poirot does however hint, in The Murder on the Links, at a more profound sense of the importance of psychology in solving a crime.

... when you have two crimes precisely similar in design and execution, you find the same brain behind them both. I am looking for that brain, M. Giraud—and I shall find it. Here we have a true clue—a psychological clue. You may know all

about cigarettes and match ends, M. Giraud, but I, Hercule Poirot. know the mind of man!'

That hint, knowing the mind of man, remains dormant. In the ten years from 1926 to 1936 Christie wrote several of her greatest whodunnits, developing her particularly sophisticated approach to plots and clues. Many of those clues involve how people behave or what they say, but they are not 'psychological' in that more profound sense of revealing the mind of man.

And then in 1936 Christie published Cards on the Table, the first novel in which we meet that fictional crime writer, Mrs Ariadne Oliver. Cards on the Table was a bold experiment that didn't quite come off. Christie was attempting a new approach to clueing, a new kind of whodunnit. Her experiment is so interesting, the set-up so good, and the character of Mrs Ariadne Oliver such fun, that we like this novel better than many that have a more satisfying solution.

The setting of *Cards on the Table* was outlined in *The ABC* Murders published earlier the same year. Christie knew that she was trying something original and was worried that readers would not appreciate it. She took the unusual step of providing a foreword. She wrote: 'The deduction must, therefore, be entirely *psychological*, but it is none the less interesting for that, because when all is said and done it is the mind of the murderer that is of supreme interest'.

At the centre of the novel is the aesthete Mr Shaitana. He is a collector of fine things, like Chinese furniture, Persian rugs, Japanese prints, and murderers: 'A murderer can be an artist ... Surely my dear M. Poirot to do a thing supremely well is a justification.' The caught murderer, he argues, 'is necessarily one of the failures. ... No I look on the matter from the artistic point of view. I collect only the best ... the ones who have got away with it.' He invites to dinner, and to a game of bridge, four people whom he thinks have got away with murder.

What Christie was attempting was to set the reader the task of identifying the murderer by matching the nature of the murder to the mind of one, and only one, of the suspects. Poirot puts

Agatha Christie learned to surf in the 1920s.



the issue clearly: 'We know the kind of murder that has been committed, the way it was committed. If we have a person who from the psychological point of view could not have committed that particular type of murder, then we can dismiss that person from our calculations.' Hence Christie's decision to make it crystal clear who are the suspects, and to limit their number to four.

Christie provides three sources of information to help the reader build up the psychological profiles of the four suspects. First, how they played bridge. Second, their past, and in particular the details around the deaths which may in each case have been murder. Third, the answers they give Poirot when he asks them to describe the contents of the room in which they played bridge.

Christie was in effect writing a novel about criminal psychological profiling, over 50 years before it became popular in fiction, in books, films and TV dramas (such as The Silence of the Lambs and Criminal Minds), and over 30 years before the first unit devoted to such an approach was set up in the FBI in 1972. Perhaps Christie knew about the attempt to use such an approach in the Jack the Ripper case in London in the 1880s. Perhaps it was simply the outcome of her developing the idea of 'psychological' clues in a whodunnit.

This experiment in psychological profiling failed as a whodunnit. No reader can be confident in identifying the murderer on the basis of matching the suspects' psychologies to the nature of the murder. More definitive clues are needed. But Christie did not give up on exploring the nature of psychological clues. Her creative mind kept thinking about the possibilities.

In Appointment with Death (1938) Christie explored the idea that the crime can be solved through an understanding of the psychology of the victim, rather than of the murderer. At the beginning of the denouement, which stretches to almost 20% of the novel, Poirot says: 'My arguments are mainly psychological'. Carbury, the no-nonsense military Englishman, responds with a sigh: 'I was afraid they might be.' 'But they will convince you' Poirot reassures him.

Despite Poirot's rhetoric, however, it is the 'factual' clues that are the key to the solution. Psychological profiling once again failed to provide the basis for a convincing whodunnit. Christie gave up on the idea. Then, in 1949, she published Crooked House. This highly original whodunnit comes wrapped in a romantic cover. The nature of the solution posed narrative problems and as a by-product of solving these, Christie wrote the most successful of her novels that involve 'knowing the mind of man'.

In the key scene the narrator, Charles Hayward, a man in his thirties, is talking to his father who is Assistant Commissioner of Scotland Yard. 'Dad', Charles says, 'what are murderers like?' In the course of his long and thoughtful answer, Charles' father says that the brake that operates with most of us to prevent us from killing doesn't operate with murderers. He goes on:

A child, you know, translates desire into action without compunction. A child is angry with its kitten, says 'I'll kill you,' and hits it on the head with a hammer – and then breaks its heart because the kitten doesn't come alive again! Lots of kids try to take a baby out of its pram and 'drown it', because it usurps attention – or interferes with their pleasures.

He goes on to adumbrate his views on the development of moral sensitivity: first children learn that things are wrong in the sense that they will be punished if they do them. Later they develop a true moral sense and 'feel' that certain things are wrong. Murderers, Charles' father is arguing, are often morally immature. In this scene Christie does most of the groundwork of enabling the reader to form a psychological profile of the as yet unknown murderer. In this novel, as in so many of her whodunnits, we see Christie combining the three principal elements of her art to form a satisfying whole: clever plots, complex clues and cunning misdirections.

Sally and Tony Hope's book Agatha Christie: Plots, Clues and Misdirections was published in September 2023 by The Book Guild Ltd.

This statue of Agatha Christie by Ben Twiston-Davies was unveiled in Wallingford in September 2023. Both Christie's husband, Max Mallowan, and her nephew, James Watts, were students at New College. Christie and Mallowan lived in Wallingford for over 40 years.



Plots, Clues and Misdirections Tony and Sally Hope

Next time you are having difficulty choosing a birthday present don't despair. Everyone has read Agatha Christie and everyone will find this book fascinating and stimulating,



The authors read each of the sixty six books three times to understand the Plot "the centrepiece of the whodunit puzzle", the Clues which "point towards the solution that the plot aims to hide", and Misdirections which "point away from the solution or conceal the clues". The book is in three sections: one on Plots, one on Clues and one on Misdirections with 11 chapters in each section. Each chapter has an intriguing title and sub-title drawing on one or more of the books to illustrate the points they are making about the "thirty three ways the Queen of Crime deceives us". The book also analyses the methods and the behaviours of the two giants – Hercule Poirot and Miss Marple.

This is a brilliant book which is both academic in the rigour of its analysis and highly entertaining. Plot spoilers are clearly signposted, so as every birthday approaches in the years to come the recipient of this book can simply be asked "which Agatha Christie would you like this year?".

Sir Muir Gray CBE MD

The Oxford Value and Stewardship Programme www.ovsp.net

Rita, the Preening Pachyderm



Paul Morrish (Wolfson College 1980), Retired Neurologist. Having initially trained as a GP, I saw a different light and it led into clinical neurology, with research, teaching and public health along the way.

It is the pantomime season ("oh no, it's not" if this is the summer issue) and a pink elephant called Rita will again grace and disgrace the Tyngewicke stage. But why a pink elephant and why Rita?

A wave of Basil Shepstone's magic wand, **Figure 1** and a magic spell "a sprinkling of stars, a hey and a ho, it's into the archive we must go" let us escape 2023 and its trumpety-Trump, and go back to the even darker days of 1939.



The first 25 years of Tingewick are documented in the archive by GE Moloney, presumably the Moloney that was Professor of Surgery in Riyadh, the author of "A Doctor in Saudi Arabia" and described by Terence Ryan thus "Ted Maloney ("operating as quickly as he eats") in a Bentley swinging speedily into the car park". Yes, young readers, doctors did once drive Bentleys. In 1939 the London hospitals were evacuated (neuroscience went to a field in Sussex) and Oxford students had to stay in Oxford for their clinical training where they were joined by London emigrés accustomed to an Xmas concert. The war heightened the need for escapism and in 1940 a pantomime, 'Dick Whittington and his Dog', Figure 2 was staged. On the last night the instigator, the same Charles Fletcher Figure 3 as gave the first dose of penicillin, announced the birth of a new society. A wild party that evening (the minutes proudly proclaim that "never before was so much drunk in so short time by so few") was followed by an unofficial committee that vowed to continue the venture. These new members spent what was left of the night carousing to the heady sounds of Guy Lombardo and his Royal Canadians' pop hit song 'Pink Elephants'. The song Figure 4 was written by Mort Dixon and Harry Woods, and you might tickle the ivory yourself at this year's Xmas party if you really have nothing better to do. It can also be heard (or herd) at https://www.youtube.com/watch?v=cgD_F1Kksgc. Thus, they called the society "The Pink Elephants" but changed



Imaqe from General Files and Country Music, 1902–1948 (series 1), Sousa Archives and Center for American Music, University of Illinois at Urbana–Champaign.

it almost immediately to Tynchwycke, after Oxford's first known medical teacher. Moloney writes that "a stuffed pink elephant was present at most meetings of the society, and a large one with human legs fore and aft has appeared on the stage". There is certainly photographic evidence of a large-eyed and smalltusked elephant as early as 1948 Figure 5.

Like Dr Who, albeit with cheaper actors and lesser special effects, Rita regenerates at regular intervals but the archive has photos of only some of the Ritas. The 70s RITA had tusks and very big eyes. In 1983 the beast was, in my un-elephantine memory, fragile and smelly yet still working in 1985 **Figure 6**. Rita was renovated for 1989 ('The Jugular Book'), with crumpled tusks and a prehensile trunk, **Figure 7**, with David Grahame-Smith writing that she was "once more in the pink, front and back. Give up the curry Rob, says Jason". Not one of DGS' better jokes; his ward-round jokes (another phrase to surprise the young) were legendary and "too many toxins" were removed from the drug charts with the stroke of a pen.





In 1990 ('A Christmas Carbuncle') she was spotted as a very elegant elephant hybrid, Figure 8 whilst the the latest, and bipedal, Rita, Figures 9,10,11 seems to attend lectures, play drums and maintain a social media presence https://www.facebook.com/rita.tingewick. In other years she has been present in head only. Figure 12, 13.

Rita has featured in every fund-raising programme, and Tingewick memorabilia is still available, as ties, bow-ties and more, **Figure 14**. One former serenity might have mused on "what pink elephant garment can be issued to lady members in lieu of the society tie?" but please don't send suggestions.

Trawling the archives, the casual unquestioned sexism of the past stands out. "Opinion at meetings has been strongly in favour of keeping the cast all male". There were officially no female members of the society until 1969 (by a vote of 7 to 5 with many abstentions). Dr Smail, the serenity who campaigned for the admission of women, recalled in 2007 that "the 1969 production marked the emancipation of women within the Tingewick society – hard to believe that it took until then to give women equality in the Tingewick society when women were first admitted to medical degrees in the UK in 1876!!" With comments like "as for the female talent in Osler House, it has to be admitted that the quantity is very limited", it is remarkable that any woman student ever wanted to take part. What an irony that, in meeting after meeting, the honorable gentlemen of









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Q: WHAT DO YOU CALL AN ELEPHANT THAT DOESN'T REALLY MATTER? A: AN IRRELEPHANT

the Tyngewick society failed to notice the presence or gender of the very female Rita, the ...er...elephant in the room. Fortunately, like trunk calls on a telephone, those days are long gone.

One peculiar aspect of the whole charade is that an actual hallucination of a pink elephant seems rare indeed in the medical literature, despite how often we hear it associated with excess alcohol or delirium tremens. A search of case reports located a single report of the hallucination of an elephant, but not a pink one and, in this case, in a patient suffering from schizophrenia. Is it too commonplace to report, or is it a myth? In the neurology world one might imagine a pink elephant appearing in Charles Bonnet syndrome or as an epileptic aura but if so, it isn't reported. Parkinson's and Lewy Body dementia patients frequently report visual hallucination but, at least in my experience, nobody ever ever sees a pink elephant. One might imagine them appearing in the phenomenology of LSD or MDMA but no, not here either. Wikipedia (no effort has been



Q: WHAT DID THE ELEPHANT SAY TO THE NAKED MAN? A: THAT'S ALL WELL AND GOOD, BUT HOW DO YOU EAT BUNS WITH IT?

spent in research for this article) argues that in the 19th century The neurological mechanism of hallucination remains unclear, reports of seeing snakes were common, and from there it was a short and imaginative step to the pink elephant hallucination. The earliest recorded written example of a (partially) pink elephant comes from Henry Wallace Phillips in an 1896 short story "The Man and the Serpent" where a drunken man sees a "pinkand-green elephant". Jack London, in his autobiographical John Barleycorn: Alcoholic Memoirs (written 1914, published by OUP in Oxford World's Classics series in 1998), describes an alcoholic who, in the extremity of his ecstasy, sees blue mice and pink elephants. For further reading and some confabulation on the evolution of the pink elephant hallucination see the blog of Peter Jensen Brown https://esnpc.blogspot.com/2014/08/thecolorful-history-and-etymology-of.html.

The idea however was sufficiently embedded in the public consciousness that Disney's Dumbo, released in 1941, featured Dumbo and a mouse (Timothy) drinking champagne and then hallucinating Pink Elephants. This was to the tune of another song "Pink Elephants on Parade" written by Wallace and Washington for the film. It is an inspired technicolour animation (though perhaps we should wonder, as the internet does, by what). The first thing that the hungover Timothy says as he wakes is "pink elephants". Dixon and Woods' Pink Elephant song was published and released by Guy Lombardo in 1932 so it must be this rather than the Dumbo song that would have been the pink elephant song of the wild 1940 party. To add to the confusion, an instrumental version of this Pink Elephant song was released in 1933 by Joe Venuti and Eddy Lang's Blue Five, https://www.youtube.com/watch?v=L2Pbjn472Bk.

Incidentally, in 2007 the Portman Group, the industry-based regulator for alcohol labelling in the UK, did not uphold a complaint from a member of the public about the use of a pink elephant on the label of an alcohol bottle. Despite Jack London, Dixon and Woods, Disney and Dumbo, Tingewick and Rita, the panel considered that the association between a pink elephant and drunken or drug-related behaviour was not well known (https://www.portmangroup.org.uk/pink-elephant/). So much for self-regulation.

and a brief wander into the literature (followed by a very hasty retreat) confirms a subject of great conjecture and intellectual torture. It certainly appears that one is more likely to hallucinate things from one's past, and thus are we all a little more vulnerable.

Moloney's account of the first 25 years, and the more recent accounts in the archive, leave many unanswered questions. The 1968 ('An Immaculate Conception') and 1969 ('Pwolapse, or Woom at the Bottom') shows feature Rita on the programme but not in the cast list. When did the Pink Elephant become Rita? Is RITA an acronym and if so, then what for? How many Ritas have there been? Who has played Rita? When did Rita start saving the day? When did she evolve from four leqs to two? If you've read this far, you'll see that the Tingewick archive is fragmented and incomplete; if this article brings back reminiscence, information or pictures that would bolster the archive please consider sending to the archive at oma@medsci.ox.ac.uk.

One can't sum up better than Jonathan Pollock, author of 50 years of Tingewick (see archive), giving the best reasons for this loveable nonsense to continue, **Figure 15**. He might also have added that it has raised a vast amount of money for good causes, but like many Tingewickian things, nobody has kept a tally.

On the last night of the Fiftieth production last December, His Munificence remarked that the spirit of Tynchwyke is a healthy corrective to our obsession with political developments in medicine. If the fifty productions have had any common theme it is certainly that we should not take ourselves too seriously. As the opening chorus of Cinderella put it:

> Cast away worry and cultivate charm, And nurture a mind like a sieve, Although we may strain to develop a brain, It's much more important to live!

> > 15

Laughter, after all, is good for you.10

Life after Medicine: Antiques



Eleanor Feldman DM (St Hilda's College, 1975) Consultant Liaison Psychiatrist/Hon. Senior Clinical Lecturer, Barnes Unit, John Radcliffe Hospital, Oxford, Consultant in Eating Disorders, Warneford Hospital, Oxford (Retired)

Pluripotent in our youth, with scope for varied interests as students, once qualified, with much less leisure time, work can become all consuming. If we're not careful, our role defines us, being a doctor becomes our identity, making it hard to contemplate letting go as retirement approaches. Fear not, life after Medicine offers us a golden opportunity to dedifferentiate.

Many of us will have had hobbies and interests that were just pursuits to amuse and relax us during time off; sometimes these hobbies become passions. In my case it was antiques, especially glass. So, when planning my retirement, it was time to set up a small antiques business.

Many antique dealers start as collectors; the pleasure of treasure hunting becomes addictive, we accumulate so much that our homes become cluttered, but enjoying the hunt, we just can't stop buying. The solution: start selling, hence the hobby morphs into a small business. Keep it small, no need to take on overheads like leasing premises or employing staff; tax affairs are simple for a sole trader with profits below the VAT threshold. You're only doing it for fun, not income....and nobody dies. You discover that a lot of the skills and attributes you used in your medical career come in handy in your new business. What are they then?

People skills

Useful in every walk of life: building rapport with customers, no hard sell, just a friendly chat much like talking to patients. This helps you discover what they want and why, so you're not totally in the dark about what to bring for sale. If renting space in a centre that employs staff, make friends with them; they will be selling your items. When negotiating a purchase be friendly to facilitate negotiating the best deal; dealers at antique fairs often have a pretty boring time and enjoy intelligent conversation so even if you don't buy but do like their items, compliment their stock, you may learn something useful from them and it may help you get a better deal in the future. When buying, asking 'what's the best for cash?' will get you at least 10 percent off unless the ticket says NT (no trade), or the item is already very cheap. Another tactic can be to allow silence to do the work; you don't know how keen the dealer is to sell or what they paid. Tolerating silence to encourage a response is a learned clinical interview skill.

Knowledge is power

Some dealers are very expert in just one or two areas but have little knowledge or interest in the rest of what they offer. This is where study skills come into play. Prior decades of collecting and handling items, visiting museum collections (including abroad), reading, and 'Googling', albeit with a critical eye, means you accumulate vast knowledge and

experience giving you an edge when buying. Add a good visual memory and you can make great spot diagnoses.

Business skills

If you've worked exclusively or mainly in the NHS, these will be something to acquire. However when it comes to tax affairs, the NHS travel claim form proves a useful template for business travel and subsistence. Stock needs to have a wide appeal, which means keeping abreast of fashions in antiques and collectibles. Understand the particular ecosystem of your market: what do competing dealers in the same space sell?, who are your customers?, what do they want?

And finally, academic skills in research, writing, and lecturing: watch this YouTube video to find out more about how I have applied these! https://www.youtube.com/ watch?v=hPBWwqfBX_U

G fear not, life after medicine offers us a golden opportunity to dedifferentiate.



'Spot' Diagnosis: Loetz vase with rare decoration of orange spots and stripes on green. Austria circa 1911. Purchased at its decorative value price for £25, sold for £375, below the full market value, so a specialist dealer could still make their margin.

Green Tips and Seeds of Hope



Dr Lyn Williamson (Thakurdas) *St Anne's College 1974 Hon Cons Rheumatologist, GWH Swindon. President Oxford Medical Alumni*

I was wrong. My prediction that very soon all articles will be prefaced with reference to the climate crisis did not happen. Call me impatient, but I could not let this edition slip through without considering our role in helping prevent the impending cataclysm.

Global problems undoubtedly need global strategies. Negotiating economic interests and entrenched behaviours requires skills and influence.

The medical community is a powerful, trusted societal group, and we are therefore well placed to advocate for change. Although 'no one snowflake believes they are responsible for the avalanche', we as individuals can be part of the solution. We control how we fuel ourselves – what we eat, and how we travel.

We can influence our own prescribing and treatment options. Positive options for eating and travel are well rehearsed, but on the ladder of behaviour changing strategies, we are not even at the 'nudge' stage (Chris Whitty 2023 Osler Lecture). However, some statistics stick in the mind, and there are some easy wins. e.g. a Salbutamol aerosol inhaler (100 doses) has the same carbon footprint as driving a car 175 miles, versus 4 miles using an equally effective dry powdered Salbutamol inhaler. This is only one drug, but there is clearly scope for meaningful

C Every time I see an adult on a bicycle I no longer despair for the future of human race. HG Wells change as globally the pharmaceutical industry accounts for one fifth of greenhouse gasses, a bigger carbon footprint than the automotive industry.

Some changes are less easy to swallow. One third of all greenhouse gas emissions come from food production. Red meat makes by far the biggest contribution. Cut out red meat to save planet? Ouch.

Last year the Planetary Health module students produced a 'green tips' page for us on ways to reduce carbon footprint of emails, diet and health care delivery. It bears re-reading.

https://www.medsci.ox.ac.uk/about-us/alumni/publications.

https://eco-age.com/resources/how-reduce-carbon-footprintyour-emails





And finally... a good news story, first to make you smile, and then to make you think.

Last year David and I received a Queen's Award for voluntary services (the equivalent of an MBE for a charity). It wasn't expected, but the recognition encourages us to share the story.

Sometime in 2018, this Youtube clip **Frozen Parkinson's Patient Cycling Skilfully** woke me up to the importance of learning to cycle in childhood, as an important life-skill. And life means life.

Two of my passions ignited (encouraging people to exercise and reducing carbon emissions), I decided to help every child in our town to learn to cycle, by chipping away

at the obstacles and excuses: nowhere to learn; no teachers; no bikes; broken bikes; parental fear and apathy. Two years later, after many hoops and hurdles, we built a 'miniature village' cycle training park; trained volunteers to teach cycling; run a cycle shop to restore, repair and sell pre-loved bikes, and have an established local cycle charity. (Farcycles).

I confess to a quiet glow of pride when I see the cycle park buzzing with children on bikes and hear parents who have travelled from afar to use it say, 'every town should have one of these'. They are right.

Congratulations

Professor Sir Peter John Barnes FRS

(Margaret Turner-Warwick Professor of Thoracic Medicine at the National Heart & Lung Institute) was awarded a Knights Bachelor Knighthood for services to Respiratory Science. His research has had a major impact on current understanding of asthma and COPD mechanisms and how current therapies for these diseases work.



Professor David Hunter

(Richard Doll Professor of Epidemiology, University of Oxford) was made Companion of the Order of Australia for eminent service to medicine as an epidemiologist, particularly in relation to disease prevention and early detection.

Professor Julia Alison Noble OBE FRS FREng

(Technikos Professor of Biomedical Engineering, University of Oxford) was made Commander of the Most Excellent Order of the British Empire (CBE) for services to Engineering and Biomedical Imaging. Prof Noble is especially well known for her work in the machine-learning based analysis of medical scans.



(Director of Global Operations, Oxford Vaccine Group, University of Oxford) was made Officer of the Most Excellent Order of the British Empire (OBE) for services to Vaccination during Covid-19. Dr Aley is responsible for the strategic oversight and direction of activity for the Oxford Vaccine Group.

Dr Giles Francis Maskell

(Consultant Clinical Radiologist, Royal Cornwall Hospitals NHS Trust) made Officer of the Most Excellent Order of the British Empire (OBE) for services to Diagnostic Radiology. Dr Maskell (Merton 1974) is a past president of the Royal College of Radiologists (2013-2016).



Professor John Norman Newton

(Director of Public Health Analysis, Office for Health Improvement and Disparities, Department of Health and Social Care) made Officer of the Most Excellent Order of the British Empire (OBE) for services to Public Health. Prof Newton (Trinity College) worked as an academic epidemiologist at Oxford and was the founding Chief Executive of UK Biobank.

Professor Sir John Irving Bell BE FRS FREng

(Regius Professor of Medicine, University of Oxford) was awarded the highest accolade, Companion of Honour, for services to Medicine, Medical Research, the Life Science Industry and to Public Health. Observant readers may have spotted that this was included as breaking news in the last issue of the magazine – an honour so good we had to name it twice.



Royal Medals of the Royal Society 2023

Professor Herman Waldmann

(Emeritus Professor of Pathology, Sir William Dunn School of Pathology, University of Oxford) "for pioneering monoclonal antibodies for human therapy".

Professor Sir Chris Whitty

(awarded jointly with Sir Patrick Vallance) for a "pivotal role in ensuring that the UK's response to the covid-19 pandemic has benefitted from the very best science and evidence".





New fellows of the Royal Society 2023





Professor Michael Dustin (Kennedy Trust Professor of Molecular Immunology, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences and Director of Research, Kennedy Institute of Rheumatology, University of Oxford)

Professor Dame Sarah Gilbert (Said Professor of Vaccinology, Pandemic Sciences Institute, University of Oxford)



Professor Irene Tracey (Vice-Chancellor, University of Oxford and Professor Anaesthetic Neuroscience, Nuffield Department Clinical Neurosciences, University of Oxford)

Oxford Medical Alumni Update

OMA promotes good fellowship amongst graduates from the Oxford Medical School by offering regular meetings in Oxford and elsewhere for continued learning, exchange of ideas, networking, and socialising.

Graduation Reunions

In 2023, OMA hosted successful reunions for 1973, 1983, 1993, 2003, 2013 and 2018 graduates this year. If you are interested in helping organise 2024 reunions, please contact lyn.williamson@medsci.ox.ac

BM BCh Graduation

In July the new graduates were conferred their degrees and celebrated with representatives from the medical school, OMA and their families and the Sheldonian and the at the Examination Schools. We welcome them to the OMA fold and wish them well in their future careers.

Career Advice for Junior Doctors – Career Mentors Needed

For young doctors seeking inspiration and advice on their future careers. OMA is keen to facilitate informal relationships around career advice. If you feel you have something to offer (we are particularly looking for consultants, GPs and senior trainees who gualified between 1992 and 2014 and are up to date with training programmes and consultant recruitment), please contact Dr Will Seligman (seligman@gmail.com).

Oxford Medical Lecture Club (OMLC)

This popular lecture series takes place at St Hugh's College on the last Monday of each month, 12.30-2pm, in person or via Zoom. For more information contact Professor John Morris: john.morris@dpag.ox.ac.uk

Future OMLC Lectures St Hugh's College

December 18 Henry Marsh: The Self-Deception of Surgeons**

January 19 Heidi de Weit: The Gut Brain Connection: recent advances & future perspectives

February 26 Peter Rothwell: The untimely death of Clinical Pharmacology: missed benefits and untold harms

March 25 Anthony Bradlow: How the Boer War 1899-1902 made the Royal Army Medical Corps fit for purpose

April 29 Rachel Clarke: The Power of the Narrative in Medicine

CLICK HERE FOR OMLC LECTURES WEBINAR LINK Webinar ID: 993 5688 8975 Passcode: 886561

Listen here to RECORDINGS OF PAST OMLC LECTURES including the 2023 Osler Lecture by Sir Chris Whitty and Weatherall Lecture by Professor Trish Greenhalgh.

** Lecture to be held at Osler House, JRH, Old Road, Headington

C Laid in the weave of personal relationships, this magazine has been written and produced entirely by voluntary contributions from alumni. Thank you to everyone. It has been a privilege. LW Ed

Recollecting Oxford Medicine

This unique oral history collection about medicine at Oxford from the 1940s onwards, inspired by Dr Peggy Frith (former President of OMA). Through a series of skilful face-to-face interviews by Dr Derek Hockaday you can listen to this special collection of memories: Please contact Lyn Williamson if you are interested in helping with taking this project forward. lyn.williamson@medsci.ox.ac.uk

RECOLLECTING OXFORD MEDICINE PODCAST SERIES

Future Contributions to Oxford Medicine

We welcome your suggestions and contributions for future articles - clinical, scientific, timely, creative, reflective, artistic, humorous. Please contact me if you would like to join the editorial team.

Editor: Dr Lyn Williamson, OMA President

Editorial Board: Dr Tim Crossley; Dr Neil Snowise; Mr David Williamson; Dr Sarah Ball; Dr Alison Rickard, Luke Williamson and Dr Paul Morrish

Update your Contact Preferences and Personal Details

https://www.medsci.ox.ac.uk/about-us/alumni/about-us.

Oxford Medical Alumni Advisory Board (OMAAB)

Lyn Williamson (President) Roger Bodley (treasurer) Dr Zoi Alexopoulou, Professor Sir John Bell, Sir Michael Dixon, Dr Lawrence Leaver, Dr Tim Littlewood, Professor Calman Maclennan, Dr David McCartney, Professor John Morris, Professor Gavin Screaton, Dr William Seligmann, Professor John Stein, Dr Catherine Swales, Dr Robert Wilkins, Miss Jewel Bennett; Dr Kevin Windebank.

IMPORTANT MEETING

Thursday JANUARY 25th 2004 4-5 pm

The linking of OMA with the new School of Medicine and Biomedical Sciences brings us the opportunity to completely review the structure and functions of OMA. If you are interested in the future of OMA and feel you can contribute, please attend, either in person or online.

OMA Annual General Meeting and OMAAB Meeting Date: Thursday January 25 2024 Time: 4-5 pm Venue: Medical Science Teaching Centre, South Parks Road, Oxford. OX1 3PL Seminar Room UGa/b

Attend in person or via zoom: Meeting ID: 962 898 9943 Passcode: 954342

Reunions 2023



5th Graduation Reunion -Somerville College September 2023

Graduating class of 2018. The first official Oxford medical fifth year reunion, at Somerville College, September

Dr Rebecca Oram, Somerville College, 2018

Meakins - MacClaran Medallists 16th **Reunion Dinner at Balliol College** September 2023

Dinner was preceded by a round table discussion about AI and the future of healthcare - proceedings from which were summarised by Scarlett Harris and Lily Watson and are featured

^{**cc**} I loved seeing old friends who I'd fallen out of touch with and hearing about what they've been up to, it was a wonderful night.

February 8th February 15th February 22nd

GTC invite OMA: Planetary Health: Law, Finance and Economic Perspectives from 5pm-6.45pm. Planetary Health and global financial stability: Jo Paisley, Richard Barker Planetary Health beyond growth: Catherine Howarth, Kate Raworth Planetary Health and legal ramifications: Jojo Mehta, Thom Wetz



Critic's Corner: OMLC Lecture Series



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

The OMLC invites distinguish, interesting and entertaining speakers to lectures which take place at St Hugh's College on the last Monday of the month from 1-2pm. To see the schedule of upcoming lectures and to watch any of these talks again please visit: https://www.medsci. ox.ac.uk/about-us/alumni/events-and-reunions/oxford-medical-lecture-club/oxford-medical-lecture-club

HIV at 40 Years Monday 26 June 2023

Professor Chris Conlon

The talk was preceded by a moving tribute to the great Professor John Ledingham, a very hard act to follow. But this month's speaker, the Professor of Infectious Diseases and Head of NDM Experimental Medicine, gave an entertaining, informative and

fascinating account of the HIV pandemic, centre-stage in the 1980s. What began as a classic detective story, finding the common links in a set of far from common presentations, led to an effective international multidisciplinary cooperative effort involving molecular biology, immunology, infectious diseases, pharmacology, affected communities, epidemiology, midwifery, paediatricsWhile HIV can now be controlled, it has not gone away; the global cost of lifetime management of infected individuals is not always offset by access to generic drugs. HIV at 40 years is a success story, but remains a cautionary tale.

Osler Lecture: the role of the State, the medical profession and the public in preventing ill health Monday 23 September 2023 Professor Sir Chris Whitty

Chris Whitty, Oxford medical alumnus, career epidemiologist and Chief Medical Officer since October 2019, became a very familiar face during the Covid

pandemic. This was a comprehensive and fascinating lecture, focusing on different aspects of health prevention in which the state can and should (or should not) play an active role, ranging from the strong public support for state measures in pandemic control to the surprisingly controversial abolition of sending children up chimneys, to the cynical encouragement of addiction in the young as a marketing tool, finishing with the rise in childhood obesity in association with deprivation. I strongly recommend watching (or rewatching) the online recording of the talk to fully appreciate this lecture.

Plants, Medicine and Magic Monday 30 October 2023 Dr Sue Burge

The speaker, a former Director of Clinical Studies at Oxford University and Honorary Consultant Dermatologist, treated us to a fascinating historical account of the medicinal use of plants. The finding of camomile and yarrow DNA in Neanderthal dental plaque suggests

that self-medication with plants goes back a long way. Modern medicine was founded by the development of pharmacopoeias over the centuries, dating at least to the 7th century BCE. Do not discount folklore! The direct extraction of pharmacologically active components of plants may be prohibitively time consuming and expensive but has been the springboard for the development of many of the drugs widely used today. Time for a visit to the medicinal plant display in the Oxford Botanic Gardens.

2023 Weatherall Lecture: **Doctors on Social Media:** Virtue and Vices in the Digital

Monday 27 November 20233

Professor Trish Greenhalgh We were treated to a fast-moving talk

by another impressive speaker, Professor of General Practice and Health Sciences. member of independent SAGE for the



Covid pandemic, and leader of a healthily large research team. The talk invited us to look at scientific truth and post-truth. doctors as conspiracy entrepreneurs, and the perils of medical orthodoxy. We were reminded that even scientists operate with "shared mental models which may serve to perpetuate flawed thinking", and that data visualisation and extended reach on social media can be used to promote false partisan narratives. Best sit back and hope for another paradigm shift, though will we ever again be able to believe what we are told?

For individual links to the videos of the lectures, please visit https://www.medsci.ox.ac.uk/get-involved/alumni/events-andreunions/oxford-medical-lecture-club and click onto each lecture title for access to the video.



Miss Jewel Bennett

(Lady Margaret Hall, 2019). President of Osler House Club, University of Oxford

" It has been an immense privilege to lead Osler House and its student body into a new academic year; and what a wonderful start it has been! "

The infamous Osler House Garden Party marked the beginning of the academic year, as hundreds of students flocked to Osler House for possibly the largest and most anticipated event of the medical calendar. Our theme was 'Medics in Wonderland' and included Queen of Heart tarts, a surfboard simulator, wood-fired pizza, live classical and jazz music, and a themed photoshoot. It was splendid to have students from across every year and entry pathway unite to celebrate a fresh start. The momentum continued into Freshers Week as the incoming students were cordially welcomed into the clinical segment of the course, embraced by their Osler Families who support the transition. The excitement was contagious and only flourished following the Osler Freshers Fair, an exhibition with over 27 societies representing both sporting and academic disciplines.

The new academic year also ushered in a dedicated committee, which I am proud to say is particularly notable for our commitment to fostering inclusivity and awareness within the student body. We have had original posters showcased for Black History Month, a Diwali sparklers night, LGBTQ+ welcome drinks, and sober-friendly socials such as the new Osler House book swap. I couldn't be



An insightful podcast spotlighting fascinating alumni who reminisce on their time at Oxford and endeavours since leaving. If you have any fun anecdotes or would like to inspire students into your field, please do get in touch!

The Clinical School Distinguished Lecturer This new annual lecture entails an informative speech by a highly esteemed fellow, followed by a formal for the speaker, Osler House Executive, and senior faculty members of the Clinical School. Tickets for the lecture will be made available for Oxford Alumni to purchase.



more grateful for their support and ideas so far.

Our William Osler House building is certainly not missing out on the action, with the Osler House Committee brainstorming practical improvements for the computer suite, mail system, coffee provisions and more! The student community have been enjoying the new interior paint decorating and gym inductions, and both the Paediatrics Society, and Obstetrics & Gynaecology Society, have already had their annual conferences in the building.

Whilst empowering those societies registered under Osler House that span decades e.g. Osler Football Club and Tingewick, we have accepted a host of new registrations including the Oxford Medical Humanities Society and Osler House Orchestra. The Orchestra have been preparing for their debut concert this December, featuring The Nutcracker Suite, Somewhere in My Memory and singalong carols. This complements other Osler festivities as the Osler Choir prepares a spectacular repertoire for the Oxford University Hospital's Carol Service. It has been an eventful term for Osler House, but this is only the beginning - we eagerly await all that is to come!

All photos are taken from the Garden Party 2023







NEW INITIATIVES

Revival of the Medical School Gazette

First published in 1947, this student-run journal holds a prestigious legacy but took a brief pause since Covid. Recently we have begun collating an experienced team to establish its sustainable revival.

'Osler Tales'...

Tingewick: An Update



Miss Toluwani Duckworth-Essilfie (Keble College, 2019) Tingewick Producer 2023-24 and 5th Year Medical Student

In recent years, Tingewick has become a huge effort to raise money for charity, with events throughout the year, culminating with the annual pantomime. In the few months since I last wrote about Tingewick we have been busy!

The current Tingewick Firm has successfully established itself and raised lots of money for Oxford Hospitals Charity and Yellow Submarine. The achievement of a group of 29 medical students is incredible.

In May we took on the 3 Peaks Challenge and, despite rain, snow and even sun, climbed the tallest peaks in Scotland, England and Wales. This was our first opportunity to bond as a Firm. Sharing trail mix and dealing with blisters whilst scaling Ben Nevis, Scafell Pike and Snowdon united us and established mutual trust. Many fond memories were made including accidentally forgetting someone at the service station!

July saw the rowers add to our charity total by rowing the 170km from Oxford to London over 3 days, an amazing effort.

Missing the spotlight halfway through the year, we began rehearsals in July and August for a September mini-production. Far from 'mini' in the end, this production ended up a full-scale show. *Charlie in the Chocolate Factory: Every Dream Starts with a DRE* saw a group of still-optimistic medical students get lost in a world of imagination, lethal CT scanners and a septic tank pipeline. Our craving for drama created enough hype to encourage the year below us to audition for their own Tingewick show.

A collective 183.4 miles was run by the Tingewick Firm in the Oxford Half Marathon in October, another incredible effort. Multiple personal bests were achieved, with our director getting a shoutout on BBC Radio Oxford for completing the race in a cardboard yellow submarine!

November is a month filled with tradition for us. The Tingewick Ceilidh returned in the stunning setting of the Isis Farmhouse where the Tingewick annual production will also take place. Over 300 people took part, the biggest ever turnout for a Tingewick Ceilidh, and it was an unforgettable night. This year's annual production is based on the Disney classic *Ratatouille*, with our beloved Rita dreaming of helping a peer pass their OSCE exams. '*Ritatouille*' took place from the 29th November to 2nd December 2023 in Tingewick Hall. Donations link is open at https://tingewick-2023.raisely.com

The approach of the pantomime signals that our time on Tingewick Firm is coming to an end but is just the beginning for our successors.

" Our craving for drama.



Tingewick2023.



Tingeaid.



Students running half marathon.

Obituaries

In Memoriam

The following deaths have been notified to the Alumni Office, since the previous Edition of Oxford Medicine

Dr. Ian H. Borton (Magdalen College, 1955) Died May 2023

Dr. Peter G. Johnson (Merton College, 1951) Died May 2023

Dr. Margaret S. Barrett (Somerville College, 1946) Died June 2023

Dr. Kenneth Hughes (Jesus College, 1958) Died June 2023

Dr. Frederick P. Greenwell (Magdalen College, 1949) Died September 2023

Dr. Henry M. Steady (St Peter's College, 1966) Died September 2023

Dr. Elizabeth K. McLean (Somerville College, 1950) Died August 2023

Dr. Ruth Lister (Somerville College, 1944) Died August 2023 GP at the Angel Hill Surgery, Bury Saint Edmunds, (1955 - 1991)

Dr. Maggie C. Eisner (Somerville College, 1965) Died May 2023

Maggie Eisner, who has died aged 75, was a GP in Yorkshire, who gave her utmost to her patients, her practice and to her young colleagues. Within her practice in Shipley she established a service for home births in Bradford and led the GP training scheme, under which many cohorts of trainees benefited from her teaching.



Full obituary in The Guardian https://www.theguardian.com/society/2023/mar/16/ maggie-eisner-obituary

Dr. Geoffrey M. Durbin

(New College, 1963) Died May 2023

Dr Geoff Durbin, who has died aged 78, was a consultant neonatologist whose early research was one of the crucial steps in improving the treatment



of babies with breathing difficulties. He was the first full-time neonatologist at the Birmingham maternity hospital. He set about developing the unit, offering, for the first time, lifesustaining support for premature babies. Full obituary in The Guardian, written by his wife, Anne Durbin, September 2023: https://www.theguardian.com/ education/2023/sep/10/geoff-durbin-obituary and https:// www.bapm.org/articles/obituary-geoffrey-mottram-durbin

Dr. Christian A. Carritt (Somerville College, 1946) Died July 2023

Christian Carritt, who has died aged 96, practised as a private GP from her home in South Kensington, London, well into her 80s, treating authors, poets and aristocrats. Her patients



included the playwright Peter Shaffer, poet John Betjeman, and authors Rosamond Lehmann and JB Priestley.

Obituary in BMJ: https://www.bmj.com/content/382/bmj. p1958 and subscription only: https://www.telegraph.co.uk/ obituaries/2023/07/30/dr-christian-carritt-medicinelondon-somerville-oxford/

Professor Richard J. Phillips

(New College, 1975) Died August 2023

Professor Phillips worked within the Faculty of Life Sciences & Medicine, King's College, London for more than 25 years, first as a Senior Lecturer and subsequently as Deputy Dean, a role he held since 2010. He contributed significantly to the Faculty's



success, helped to launch the careers of thousands of medical students and he was also a valued mentor to many educators within the GKT Medical School. https://www.kcl.ac.uk/news/ a-tribute-to-professor-richard-phillips

Dr. Tim Lancaster (Corpus Christi College, 1974) writes: 'I met Richard when I moved from Oxford to King's, as Dean of Medical Education, in 2017. We worked in adjacent offices and he often dropped by to offer advice, share his deep institutional memory, and encourage at difficult moments. He was a wonderfully kind and insightful man, generously committed to supporting students and fellow faculty.'

Roy L. Bishop (St Edmund Hall, 1983) Died August 2023

Dr. Bishop completed his medical training at Glasgow University, before becoming a General Practitioner. As a GP he worked in Stirling and on Benbecula in the Outer Hebrides.In the late 1980s, he joined the regular British army, training as an officer at Sandhurst. He subsequently



Obituaries

emigrated to the USA and poured his considerable intelligence and energy into building his own private medical practice, the Argyll Medical Group.

A full eulogy to Dr. Bishop will be available on-line, from December 2023, in St. Edmund Hall 'The Magazine' at https://www.seh.ox.ac.uk/alumni/publications

Professor Franklyn G. Prendergast (Lincoln College, 1969) Died October 2023.

Professor Prendergast qualified in medicine from the University of the West Indies, in 1968. He was a Rhodes Scholar in Oxford, before moving to the USA for the rest of his career. Of his many achievements, he became director of research at the Mayo Clinic and subsequently, in 1995,

he was appointed Director of the Mayo Clinic Comprehensive Cancer Center, a position he held until 2006. He received many accolades and has been described as having a brilliant mind, while being a dedicated physician and extraordinary person.

Further information: https://cancerletter.com/ obituary/20231020_5/

Professor Vincent Marks (Brasenose College, 1948) Died November 2023

Professor Marks spent several years working in laboratory and metabolic medicine, where he developed his interest in hypoglycaemia at the Hospital for Nervous Diseases. In 1962 he became

the first consultant in chemical pathology at Epsom district hospital. In 1970 he became foundation professor of clinical biochemistry at the newly established University of Surrey. His Guildford laboratory was the first in the UK to offer insulin assays to NHS hospitals. He was a pioneering researcher into insulin and hypoglycaemia and a much sought-after expert witness in many infamous trials. He helped to secure the conviction of British child killer Beverly Allitt and the acquittal of Claus von Bülow, the playboy lawyer originally convicted of killing his heiress wife by injecting her with insulin, which was one of the 20th century's most sensational court cases and the first major US trial to be televised.

Full Obituary: https://www.thetimes.co.uk/article/professorvincent-marks-obituary-xrr0smzdf and https://www.bmj. com/content/383/bmj.p2750.short

Dr. Hassia A. Orgel (Lady Margaret Hall, 1947) Died March 2022

Born in 1929 in Lithuania, her family fled to London, when she was aged four, due to growing fears of a Russian invasion and anti-Jewish sentiment that was stirring with the rise of the Nazis

in the region. Dr. Orgel was accepted by the University of Oxford to study medicine. She graduated in 1950 and continued her studies at Oxford, receiving both an M.D. and Ph.D. Dr. Orgel was in one of the early classes of medical school students that included women. In 1964, she moved to La Jolla, California, with her husband, where she practiced medicine at Allergy & Asthma Medical Group & Research Center as a paediatric immunologist and allergist.

Obituary: https://www.legacy.com/us/obituaries/ encinitasadvocate/name/h-orgel-obituary?id=33958559

Dr Nick Leigh-Hunt (1972-2023)

A tribute from his wife, Dr. Sabrina Leigh-Hunt, Consultant in Old Age Psychiatry, November 2023

Nick was educated at Harrow School where he was awarded an L.C. Wilson scholarship and he went up to Merton College in 1991 to

study Medicine. For his clinical training he went to Guys' and St Thomas's Hospitals, where we later met.

Nick was diagnosed with Multiple Myeloma in 2003. He carried his illness with great dignity and privacy. Originally, he intended to be a paediatrician and Nick obtained his MRCPCH and Masters in Child Health in 2008, at Leeds University.

He later embarked on a career in Public Health and undertook a Masters in Public Health in 2011. Nick worked as a Consultant in Public Health at Rotherham Metropolitan Borough Council, where he led on all things Healthcare Public Health, developing strong relationships with Rotherham CCG and the local NHS providers. His systematic review on the public health consequences of social isolation and loneliness became one of the top cited and most read articles in the Public Health Journal. Towards the end of his career, he played a vital role in Rotherham's response to the Covid 19 pandemic, providing clinical guidance for health and care settings, supporting schools and workplaces to manage risks. During what was a difficult time for Public Health and for Nick personally due to his vulnerability to infection he delivered this role with his usual academic rigour, compassion and diligence. He retired in 2022, due to a recurrence of his myeloma.

Nick travelled extensively around the world. He loved learning from people and getting to know different cultures. He spent time in Africa during his gap year and Sudan during his elective. He had a passion for walking, especially in Yorkshire, Scotland, Wales and the Lake District. Nick was an excellent gardener and an avid reader. He passed these passions on to his daughter Sophia. He was very modest, kind and thoughtful to those around him.

A devoted family man with great professional integrity, and loyalty to friends, Nick was widely admired and will be greatly missed.

Dr Martin Moncrieff (1933-2023)

Martin Moncrieff was educated at Marlborough College, Oriel College and, for clinical training, the Middlesex Hospital. As the son of a distinguished paediatrician (Professor Sir Alan Moncrieff, the first Nuffield Professor of Child



Health at the Institute of Child Health and Great Ormond Street Hospital), he expressed no concern for the potential advantages or disadvantages this might bring and, after National Service with the RAMC, developed a career in paediatrics himself.

As a Senior Registrar at Birmingham Children's Hospital with Richard White, he was involved with the early development of paediatric nephrology and was one of the eight founding members of the British Association of Paediatric Nephrology, the so called 'Dublin Eight' because of their inaugural gathering at a European conference in Dublin in 1972. His first consultant post was at Derby Children's Hospital where he was busy and happy but, in 1976, he was persuaded to move to Oxford, where paediatric services were still based both at the Churchill Hospital and the Radcliffe Infirmary.

Paediatricians of the 1970s were few, had onerous on-call commitments, and had to be skilled in the care of the newborn as well as older children although the development of the neonatal service under Professor Peter Tizard at the new John Radcliffe Hospital relieved Martin of neonatal responsibilities when he arrived in Oxford. However, he remained the cornerstone of the provision of general paediatric care and while he had brought special expertise in paediatric nephrology when he came to Oxford, it was difficult for him to develop this as a major component of his working life. Instead, by the early 1980s, he had acquired responsibility for an entirely different area in the emerging speciality of paediatric haematology and oncology. It was still a time when some in the paediatric world retained a degree of therapeutic nihilism about the possibility of treating children with cancer. Yet, without specific training and in a relatively short time, Martin had developed an effective service for children with leukaemia and other kinds of cancer. Supported by Pauline Emerson, an adult haematology colleague, leukaemia care was delivered almost entirely in Oxford whilst children with so called solid tumours were managed jointly on a shared-care basis with the team at Great Ormond Street. These were challenging times but paradoxically felt like good days.

Consultant colleagues recall his interest in their own careers, and of his quiet support for those in times of personal difficulty. He was once said to have declared in the department that everyone should have at least one skiing holiday a year – and in doing so illuminated his recognition of the importance of work life balance. Trainees spoke of his kindness and his willingness to let them learn by taking decisions. Parents of his patients recall him with respect and gratitude and, for the children, he was a gentle doctor with a kind smile and the essential ability to show ageappropriate connectivity. In reflecting on his career, Martin felt fulfilled: he had enjoyed the work he had done and was happy with the contribution he had made.





As an undergraduate Martin had been a very good squash player; he continued playing to a high standard far longer than most. But his happiest times were in mountains, in France and at his home near Oxford. He had climbed the Matterhorn as a young man and was skilled on alpine glaciers, ski slopes and mountain trails. In retirement he undertook a full-time undergraduate degree in French and enjoyed his many visits to France. With his wife Ann, he shared a wonderful family house and garden with their four children, and the later generation of grandchildren, of whom he was quietly proud yet modest about their achievements. After experiencing declining health in his last few years, Martin died at home with his family by his side.

Professor Mike Stevens and Dr Roy Meadow

John Gerard Garvin Ledingham, FRCP

(1950, Fellow 1974, Honorary Fellow 2000) (1929 - 2023)

Entering New College in 1950, he first read Physiological Sciences and then Clinical Medicine in 1954.

Appointed in 1966 as consultant physician for



Regius Professor, George Pickering, John devoted his life to the Oxford Medical School, propelling it steadily towards preeminence. Combining sharp understanding of science with intuitive curiosity about people, he assembled and motivated a team of talented and committed clinician scientists. When he had arrived at New College in 1950, Medicine was held in low intellectual esteem. John, though, habitually selected keen students as undergraduates and DPhils, then steered their interest to areas he identified in ward and clinic; many rose to positions of distinction, often returning to Oxford.

Eminent medical parents tried to dissuade him. Perhaps his exposure to Classics at Rugby School destined him via Greats 'for a jolly career in schoolmastering'. But as a junior infantry officer in Hong Kong, 'flattening paddy fields into a runway' ideal for hockey, he became intrigued by Baldwin's Dynamic Aspects of Biochemistry and decided to change to Medicine. Before Finals, too many lunches at Vincent's led to 'a panicked invasion of the Physiology laboratory to bone-up on a frog sciatic nerve experiment, where the diminutive tutor Jean Bannister discovered this very keen young man beavering away'. He fielded both a Hockey Blue and a First.

His chosen subject came as a revelation; 'I was gripped and transformed by clinical medicine' when he moved to the Middlesex for hospital training. Pragmatic observation and logical deduction, with intuitive leaps and often some urgency, inspired him in a way which never faded. Demanding days as a trainee at the Middlesex and Westminster hospitals gave him first-hand responsibility and experience with many eminent role models to hone the accuracy of his thought and action. He gave humane care to a wide spectrum of patients in the early days of the NHS, with shrewd yet compassionate understanding of the patient's complex relationship with their illness.

Obituaries

A DM led to work with John Laragh in New York, challenging the role of aldosterone in high blood pressure. He 'walked across Washington bridge to the lab to save half a dollar for a babysitter as we were living just below the poverty line'. Laragh had 'a maniacal interest in blood pressure and golf, and was very competitive, very good-looking, with a very lucrative private practice of women in diaphanous nighties'. But 'measuring endless plasma renin levels in the lab proved very lonely'.

Laragh and George Pickering's shared interest in hypertension ushered in his Oxford appointment and with the advent of dialysis and transplantation he specialised in the kidney. He was always 'the doctors' doctor' to whom colleagues might turn in a fix over any difficult case. At Grand Rounds he kept everyone on their toes as his eagle eye would spot some key aspect others had missed. His DPhil/MD students included Peter Ratcliffe, Nobel destinate, who at JGGL's suggestion looked at 'why on earth the oxygen sensing molecule EPO is in the kidney'. Peter says 'There are two types of mentor, those who give advice on the what to do, and those who provide confidence to do what you want. John was of the latter, infinitely better, type. I'm for ever grateful for his support.'

John was Director of Clinical Studies twice and always championed students with a sometimes reluctant University hierarchy, steering the move from the Radcliffe to Headington and a new Osler House. He enticed students from Cambridge which lacked a clinical school. Oxford University Press challenged David Weatherall to produce a textbook of Clinical Medicine which was 'actually interesting' and, co-opting John and David Warrell, they achieved quasi-biblical success. He was made Honorary Fellow at New College, which 'gave him his greatest pleasure', and was recognised as a Distinguished Friend of Oxford - the students' affectionate ditty 'Here's to you Professor Ledingham' qua Simon and Garfunkel reduced him to tears.

He shared attributes with his mother Una, pioneer London teaching-hospital consultant, described as having 'brilliance and empathy, intelligent, gifted, and with tireless energy'. His medical wife Elaine supported him with much wisdom and great warmth of family life and he was immensely proud of four daughters 'all working successfully with people in the real world'. He was a notable and respectful sponsor of women clinicians - as mentor he was amusingly supportive, if sometimes less attentive in listening! He was amused by personality traits of his colleagues and would literally crease with mirth at ironies, absurdities and personal foibles, with particular aim at the pompous. He was unfailingly appreciative of those who worked harmoniously behind the scenes as secretary, cleaner, porter, butler, or administrator.

Asked if he was ambitious he thought 'not if it meant trampling on others', though perhaps performance anxiety dissuaded him from formal high leadership. His true strength lay in giving inspiration and confidence to those who accompanied him on the medical journey.

Dr Peggy Frith, Medical Ophthalmologist (retired), former President of OMA

This tribute from his 1981 house physicians speaks for many of us:

'Dear John, Many of us were lucky enough to benefit from your many extraordinary talents, especially those of us who worked

with you in the NDM. You are a brilliant physician, clinical teacher, diagnostician, researcher, and author. You have also been a generous, funny, compassionate, and approachable mentor, who provided wise counsel to thousands of former students, including many professors, distinguished figures of the medical profession and, indeed, laureates. In true Socratic tradition you always know how to ask the right questions. Stimulated us to think and learn for ourselves. You will never know how many careers you have inspired, and how many lives you have touched.'

Mary Ryan and Lyn Williamson HPs 1981

John Ledingham was a commanding presence in Oxford medicine for nearly three decades. He was the archetypal general physician not tied to the routines of a medical specialty. This suited his eclecticism, his tendency to fill his in-tray with too many tasks for a day, and his gregarious nature. He could joust with the medical specialists, the surgeons and the scientists too. He loved Oxford, with its clubby social mix, centred for him on New College where he was a Fellow. In 1974 he was appointed to the May Readership in Medicine. He was the ideal wingman for Sir David Weatherall the newly appointed Nuffield Professor of Medicine, a haematologist. This post provided Ledingham with a platform for his broad range of skills and energy allowing him to contribute locally and nationally to the NHS, the Oxford Clinical School, research and education. The University awarded him a Personal Chair in Medicine in 1989. He was so content in Oxford that he politely declined a number of approaches to move elsewhere. This was just as well for he was not temperamentally suited to the ruthless and lonely task of running a big department. He was too kind. EJR Burrough describes him as "A Percy Blakeney" of the world of medicine. He was the synthesis of the bedside doctor and the scientist; both sometimes fighting simultaneously to gain ascendancy. His natural aristocratic and equally natural common touch did not have to fight; they were joined and presented a united front. He had that rare capacity to be caught up in his patient's predicament yet professionally to stand aside- clinically to support him in his life and personally to mourn him at his death. He too had a kindly, scandalous repertoire about events and people which showed a fine and often hilarious perspective."

He was born on the 19th October 1929 in London. son of John and Una (Garvin) Ledingham. His father was a general practitioner and his mother a physician at the Royal Free Hospital. His maternal grandfather was JL Garvin, the editor of the Observer which may be why John was said to have described his dream job as editor of the Guardian. In retirement he, with Mark Pottle, edited his uncle Gerard Garvin's 1914-1916 correspondence from the trenches in France with his parents. The book "We hope to get word tomorrow – the Garvin family letters" was published in 2009. Gerard Garvin was killed the day after his father had written that line. John, born 13 years later bore his names. He was educated at Rugby School and was minded to read Classics. During national service as a Second Lieutenant in the Royal Artillery in Hong Kong, he changed his mind, immersed himself in physics, chemistry and biology and switched from Classics to Natural Science prelims at New College Oxford. He graduated BA with 1st Class Honours in Animal Physiology. He was awarded a Blue for hockey in 1954 and went on to captain Scotland in 1957. He was a clinical student at the Middlesex Hospital. After qualifying in 1957 he was awarded the MRCP in 1959 and made a Fellow in 1971. He worked in junior

posts at the Middlesex Hospital and was registrar to Sir John Nabarro (diabetes and endocrinology), the Whittington Hospital (neurology), and finally Senior Registrar to Dr RIS Bayliss and Dr F Dudley Hart at the Westminster Hospital from 1962-4. This Firm exposed him to endocrinology and rheumatology and, as was the custom, general medicine. He had flirted with neurology but chose to pursue his undergraduate interest in the kidney stimulated by reading Homer Smith's Comparative Physiology of the Mammalian Kidney. He learnt the technique of renal biopsy from Dr Joe Joekes. He obtained a research fellowship at Presbyterian Hospital, Columbia University, New York City, 1965-1966 where he worked with Dr John Laragh on the role of the renin-angiotensin system in hypertension. Having failed to be appointed to a consultant post at the Middlesex he was invited to apply for one of two new posts in general medicine, endocrinology, diabetes, metabolic medicine and nephrology in the United Oxford Hospitals. He and Dr Derek Hockaday were appointed, John became part of the Lee, Ledingham, Juel-Jensen firm on the insalubrious WW2 hutted wards, Rowney and Alexandra. at the Radcliffe Infirmary.

He was first a clinician - he relished his outpatient clinics, on-take and referrals from colleagues. He made patients feel special by listening and promising to seek a solution. He was loyal to them and they were devoted to him. His registrars tired of being asked, "But where is Dr Ledingham?". His career was packed with roles, tasks and interests. His charm, enthusiasm and fluency led to an array of invitations to do and serve and he found saying `No` difficult. His unrealistic schedules often made him late for starts but he always apologised, blaming something unexpected or someone who had been too prolix. We suspected that he may have been referring to himself. He made a major contribution to the expansion and reputation of the Oxford Clinical School which enjoyed a golden age after the appointment by Sir George Pickering and later Sir Richard Doll (the Regius Professors) of a number of academic clinicians. He was twice the Director of Clinical Studies - the benign shepherd of a generation of medical students who modelled themselves on his clinical method and were stimulated by his style of teaching – challenging dogma and encouraging enquiry. He was a fair and gentle BM examiner and was delighted when the Ledingham Prize was created to recognise the best Finals student in clinical medicine. In 2011 the University awarded him the title of Distinguished Friend of Oxford.

With Dr Desmond Oliver he had started the Oxford Renal Unit in 1967. This required that the consultants set up the dialysis machines. Early on they had to seek the help of a patient who from another bout of aspiration pneumonia which he declined had learned at the Royal Free Hospital how to dialyse at home. to oppose. While Oliver was mastering the technical challenges, Ledingham Chris Winearls D.Phil. FRCP, Consultant Nephrologist (Retired) turned his attention to the horrible complications of renal failure – recruiting John Kanis, Michael Bishop and Bob Henderson to work on renal osteodystrophy, and later Raman Gokal on We honoured Professor Ledingham with a birthday anaemia and Prof Gwynne Thomas and Barry McGrath on tribute in the June 2020 edition of Oxford Medicine hypertension. He was by his own admission not cut out to run a https://www.medsci.ox.ac.uk/about-us/alumni/ research programme but enabled others to do so after suggesting publications. He was one of the first to take part in problems for investigation. He drew Gwyn Williams, Peter the Recollecting Oxford Medicine Interviews. He gave Ratcliffe, Anthony Raine, Christopher Pugh and John Firth, into 2 contrasting interviews and you can listen to him nephrology and all five went on to successful academic careers. in his own voice: https://podcasts.ox.ac.uk/john-He was known as an ideal mentor. He inspired confidence, was ledingham-0 kind, exercised appropriately his power and influence, and gave advice, not commands. His own longstanding interest in the renin-angiotensin system was rewarded with the opportunity to

investigate the use of captopril in resistant hypertension, neatly described by his then registrar, Nicholas White, in the Lancet in 1980. His broad interests made him an excellent Chairman of the Medical Research Society, Secretary of The Association of Physicians of Great Britain and Ireland, and President of the British Hypertension Society. He served on the Executive of the National Kidney Research Fund (now Kidney Research UK). He much enjoyed being a Trustee of the Beit Trust advising on scholarships and infrastructure awards to Zambia, Malawi and Zimbabwe. He was a founding Editor of the Oxford Textbook of Medicine – probably the best clinical textbook of medicine in the English language. It is now in its 6th Edition and edited by two of his protégées – Dr John Firth and Prof Tim Cox. He served the Royal College of Physicians as Censor 1984-5 and as an MRCP Part II examiner for eighteen years. His reputation for common sense ensured invitations to serve on various bodies dealing with animal experimentation, the bioethics of xenotransplantation and coronary disease prevention.

In 1961 he met Elaine Maliphant, "a Cardiff girl", also from a medical family (her father was an obstetrician). She was herself a doctor working at the Middlesex, specialising in Obstetrics and Gynaecology when they met. They became engaged within 6 weeks and married six months later on March 3rd 1962. Her relaxed warmth, natural intelligence and informal nature was a perfect fit for him. Their mutual love of music, particularly opera, enriched their marriage greatly. Together they did much for Oxford's links with the Welsh National Opera. He described her as the person who so enabled his professional and family life that he could not bear to be without her. He felt guilty in later life, that she put her career second to his, but every indication suggests that she relished her role. Sadly, she predeceased him, dying in 2019. He cared for her and bore the loss of her person and her life bravely, supported hugely by old colleagues and friends. They had four daughters who helped shape his attitude to women. He championed women at work and at home, nurturing any interest they had and supporting them both practically and with words of humanity and wisdom through their various trials. Joanna Ledingham became a consultant rheumatologist (and later President of the British Society for Rheumatology), Catherine (Marsh) a teacher and farmer's wife, Clare (Bowron), a fiction editor at Penguin and Sarah (Coupe), a physiotherapist.

Retirement in 1995 allowed him to pursue his passion for music, history, golf and fly-fishing. To his annoyance a succession of afflictions robbed him of his mobility and independence but thankfully not his mind, still pretty sharp until the end which came





Kingfisher

c Dr John Reynolds (St Catherine's College, 1975) former Consultant Physician and Clinical Pharmacologist

Kingfishers are reasonably common in the UK and with a bit of persistence can be found on most waterways. In the winter they move away from breeding areas and you can even see them from Hythe Bridge Street along the Oxford canal. They may draw attention to themselves with a high pitched whistle as they streak away in a flash of turquoise low above the water.