Letters to the editor

Predatory journals

Since you published the article about my grandfather[1] I have been on the receiving end of dozens of messages from journals such as you discuss in your fine editorial with Dr Misra.[2] At first I was flattered that their editors should think me qualified to offer 'research' on subjects ranging from rheumatology through orthopaedics and sports medicine to geology, then just amused. Some of them asked me to produce an article within a few days 'for the next issue'; publication charges would be relaxed and maybe I could be appointed to the editorial board. Many of these journals, I concluded, would not last long. Where I disagree with your editorial is in your suggestion that scientific publishing has only lately been muddied by commercial considerations. For some medical bodies the 'house' journal has long been an important source of funds, and editors have come under recurring pressure to allow exploitation of a journal's 'brand'. In my day on the International Committee of Medical Journal Editors one of the biggest issues was the 'special supplement', usually to be sponsored by a pharmaceutical company. It was truly difficult to ensure that these publications, whose format closely resembled that of the regular journal, would conform to the usual editorial standards. A dispute about branding caused the *NEJM* (owned by the Massachusetts Medical Society) to lose an editor-in-chief, Dr Jerry Kassirer.[3]

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COVID-19 pandemic and the hidden front line

Military language has been frequently employed to describe healthcare's approach to the COVID-19 pandemic with talk of 'battling' the virus on the 'front lines' of National Health Service (NHS) hospitals.[1] We know that palliative medicine is not the first setting brought to mind when we talk of front lines, but just like emergency services, hospices had to adapt quickly to the challenges brought on by COVID-19.

As the NHS in the UK sought to increase bed capacity for the influx of COVID-19 patients, we began admitting a larger number of frail patients for end-of-life care who would ordinarily have remained in hospital or have been discharged to a care home. The numbers of patients admitted to hospices for symptom control or for respite for their families plummeted, mirroring the reduced uptake of acute services in hospitals for conditions other than COVID-19. For the hospice, this meant the largest turnover of patients seen in months with many living only a few days or even hours after admission. The hospice felt like a 'death machine', where people were entering moribund or barely conscious and leaving in coffins. We were often unable to connect with their families, or develop an understanding of their wishes and concerns. There were days when our mortuary was full to capacity with patients dying faster than they were able to be removed by PPE-clad undertakers.[2]

Moral injury – a term again coined within the armed forces – describes the psychological distress caused to the individual when their actions, or lack thereof, violate their own moral or ethical code.[3] It has been described in healthcare workers during the coronavirus pandemic. For our team, the cause of distress was not a lack of available beds or the rationing of ventilators but rather a clear mismatch between what we knew to be good palliative care and what we were able to provide for patients. Anxious, dying, COVID-19 patients were isolated, their only interaction being with masked doctors and nurses who had been told to limit their time in the rooms. Patients lost myriad complementary therapies: dog therapy, chaplaincy input, psychosocial therapies and bereavement support. The menu of holistic management options normally available to us was suddenly withdrawn. We were forced to have new, challenging conversations with patients behind layers of PPE.

Though it looks as though we have now weathered the worst of the storm, it is clear that the turbulence caused by coronavirus within hospices will continue for many months to come. We are seeing glimmers of hope of a return to some normality but as junior doctors working in palliative care we feel that we are just beginning to catch our breath and reflect on the trauma of the last few months on this … our hidden front line.[4]

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Relevance of the lymphocyte content of a tuberculous pleural effusion

The observation that 'This low ADA (adenosine deaminase) was inconclusive to consider the possibility of tuberculosis despite being a lymphocytic exudative effusion'[1] deserves further elaboration given the observation that 'the enzyme ADA-2 is elevated significantly in pleural fluid with activated lymphocytes, such as from tuberculosis'.[2] Indeed, two examples of the occurrence of normal ADA (<40 U/l) in tuberculous pleural effusions (TPE) were from patients who did not have a predominance of lymphocytes in the pleural effusion but, instead, either had a predominance of polymorphs[3] or a predominance of mesothelial cells in the pleural effusion.[4] In one of the two patients the TPE was initially left-sided, and characterised by lymphocyte predominance in association with an ADA concentration of 64 U/l. Subsequently, the patient developed a right-sided exudative pleural effusion with a neutrophil predominance and an ADA concentration of only 21 U/l. Nevertheless, GeneXpert evaluation of the right-sided effusion generated a positive result for a tuberculous aetiology.[3] The other patient had a high mesothelial cell content in the pleural effusion, but no mention was made of the lymphocyte content. In spite of an effusion which tested positive for *Mycobacterium tuberculosis* on polymerase chain reaction, evaluation of the pleural fluid ADA concentration amounted to <8 U/l.[4]

A more complicated relationship between ADA concentration and lymphocyte content of TPE seems to emerge from the study by Kim et al.[5] In the latter study, there were 16 TPE cases in whom the pleural effusion initially had a predominance of neutrophils. In that subgroup three of the patients had an initial ADA level of <40 U/l. The other 13 patients had ADA levels amounting to >40 U/l despite having a neutrophil predominance in the pleural effusion. In one of the three patients with an initial ADA of <40 U/l, the ADA increased to 100 U/l when the pleural effusion became predominantly lymphocytic. However, in the same study, there were seven other TPE cases in whom the initial ADA concentration was <40 U/l despite the fact that the effusions had a predominantly lymphocytic content. In five of those patients a follow-up sample of pleural fluid was characterised by an increase in ADA concentration to >40 U/l.[5]

In the latter study, criteria for the diagnosis of TPE comprised one of the following:

1 A positive culture for *M tuberculosis* (MTB) in the pleural fluid, pleural tissue, sputum or bronchial aspirate.
2 Pathological chronic granulomatous inflammation with either a positive MTB polymerase chain reaction, positive acid-fast bacilli (AFB) smear or caseous necrosis in pleural biopsy tissue.
3 Chronic granulomatous inflammation alone in the pleural biopsy and pleural effusion that resolved with anti-TB treatment.[5]

These studies show that TPE with lymphocytic predominance can have ADA concentration amounting to <40 U/l. However, in some cases an ADA concentration amounting to <40 U/l appears to be associated with a low lymphocyte concentration in the pleural effusion.

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Author's reply

We thank Dr Jolobe for his valuable comments about our case report. As pointed out by him, adenosine deaminase (ADA) levels are usually more than 40 U/l in tuberculous pleural effusions. ADA levels less than 40 in lymphocytic pleural effusions almost rules out tuberculosis in low-risk areas (prevalence of TB <125/100,000 population), implying a negative predictive value of 99%.[1,2,3] But in high-risk populations like India these cannot be used as exclusion criteria as low ADA levels are observed in about 7% of tuberculous pleural effusions.[4] This is the reason why we had quoted that low ADA in our report as inconclusive.

Dr Jolobe has quoted studies of tuberculous pleural effusions with low ADA and noted that it can increase later suggesting the need for repeating ADA measurement. In older patients and critically ill patients with tuberculous pleural effusions, ADA levels can be low.[5] The purpose of our report was to highlight tuberculosis as one of the important causes of hypercalcaemia in a country such as India with high prevalence of TB. The relevance of low ADA lymphocytic pleural effusions has been evaluated in many studies. A group in Spain showed that patients with idiopathic pleural effusions could be followed without therapy for tuberculosis if the ADA level is <43 U/l.[6] There was no evidence of reactivation of tuberculosis in ten years of follow-up despite 50% of the

subjects having a positive purified protein derivative test. In our case hypercalcaemia was the clue which led to whole-body PET as part of evaluation. PET showed diaphragmatic lymph nodes which were biopsied and histopathologically and bacteriologically proven to be tuberculosis.

To summarise, low ADA in lymphocytic pleural effusions cannot rule out tuberculosis in countries with high prevalence of tuberculosis as it can be an atypical presentation of tuberculosis.[7]

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Bedside echocardiography – are medical trainees falling behind?

Soon after the *Titanic* disaster, in 1915 Langevin[1] developed the SONAR (sound navigation and ranging) system to detect submerged objects. Since, the power of ultrasound has been harnessed and is a key diagnostic tool for physicians and surgeons alike. The last decade has seen further advances, with echocardiography (echo) probes that plug directly into your phone. Focused echo is gaining increasing popularity with intensive care and emergency medicine trainees. However, I believe it remains underutilised in medical training.

Described by a particularly enthusiastic consultant of mine, bedside ultrasound should be used as an 'extension of your stethoscope'. Not to replace formal examination, to enhance it. The Intensive Care Society's FICE course[2] (focused intensive care echocardiography) teaches how to identify cardiac tamponade, severely impaired ventricular function, regional wall motion abnormality, pleural fluid and inferior vena cava filling.

There are several key advantages in training a medical doctor to use an echo probe. Admissions and unwell inpatients can be assessed quickly and thoroughly. Its utility in diagnosing reversible causes for cardiac arrest is well documented[3] and its use is included in Resuscitation Council guidelines.[4]

Bedside echo is not reserved for the cardiologist or intensivist. Echo training provides a heightened awareness of physiology and a better understanding of formal echocardiography reports. Alongside this, inpatient echo is a service that is often overwhelmed and can frequently cause delayed discharges. In the hands of a well-trained physician, focused echo can help triage requests.

These skills can be extended to the use of ultrasound elsewhere. Lung ultrasound is arguably a simple yet underutilised practice that can aid in medical assessment and ensure safe chest drain placement. The evolving COVID-19 pandemic has highlighted the utility of lung ultrasound in patient management.[5] In fact, lung ultrasound has been found to have superior sensitivity when compared with chest X-ray for diagnosing pneumothorax.[6]

Echo is operator dependent. Image acquisition can be challenging and interpretation difficult. As with any skill in medicine, an understanding of its limitations, safe interpretation and reporting are vital. Education, supervised sessions and time performing log-book scans are vital in training a safe practitioner. It is important to have adequate supervision, information governance and quality assurance practices in place to ensure safe practice.

Courses such as FICE offer structure. However, accredited trainers are often hard to find and overwhelmed by trainees. During my FICE training, I found echocardiographers were excellent teachers. If funding allowed, I believe they would be an incredibly valuable resource.

Integrating bedside ultrasound more closely with the medical training curriculum would help ensure structure and quality assurance in echo training. Incorporating ultrasound into internal medical training (IMT) study days and funding sonographers to provide education and supervision would enable more medical doctors to develop this key skill.

Medicine is changing. As millennials and generation Z become our medical trainees, let's sate their appetite for technology (and increase their skill set) by extending their stethoscopes.

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Will COVID accelerate the trend towards greater usage of laboratory medicine, in place of clinical skills?

In many areas of life COVID-19 has accelerated underlying temporal trends – such as the shift from high-street to internet shopping and, in medicine, the greater use of remote, internet-based clinical consultation. We suggest that COVID-19 will accelerate another trend in medicine – clinicians becoming more reliant on laboratory testing.[1]

Three successive lockdowns in the UK have significantly interrupted the time available to medical students for clinical bedside learning. Following the first wave, many medical schools took urgent action to graduate final year students, often earlier than usual, to help with the crisis. The third, and latest, lockdown will further truncate bedside learning. Medical students who were in their penultimate year when the epidemic broke will have had half of their intensive clinical-based training (considered years three to five of medical degree) impacted by COVID. Four-year graduate entry programmes have less time overall and have a higher proportion of clinical exposure than more traditional courses. They will be proportionately more affected.

Medical schools have compensated for the interruption to clinical attachments by maximising online resources and, where possible, using simulation to support learning – but these cannot fully compensate for the ability to elicit the patient history and examine for clinical signs at the patient's bedside. As William Osler wrote, 'Medicine is learned by the bedside and not in the classroom. Let not your conceptions of disease come from the words heard in the lecture room or read from the book. See and then reason and compare and control. But see first.'

We believe that a consequence of less reliance on clinical skills will be greater use of laboratory medicine in the initial approach to diagnosis – rather than to be used to adjust the pre-test probability, formed in the doctor's mind from the clinical consultation. Such a greater reliance on laboratory testing has been observed over the last decade and more.[1] The causes for this are multifactorial but likely relate to the technological evolution of healthcare, with blood analysers now capable of processing thousands of samples every day at a fraction of their former cost; the ordering of large numbers of tests may be driven by the fear of missing important clinical details and the potential for subsequent litigation. Clinicians may also misconstrue the high precision and reliability of a test with diagnostic accuracy.[2]

Overuse of laboratory tests has a significant cost implication and can subject patients to direct harm, such as from subsequent radiation exposure; as well as overdiagnosis and psychological stress.[3] In view of the reduced time for developing bedside clinical skills, we suggest that medical schools urgently bolster the medical school and foundation years training of laboratory test performance, covering pre- and post-analytical error, sensitivity, specificity and predictive value of a test – as well as understanding Bayesian reasoning in decision-making. In this way, the laboratory will indeed be a useful servant and not a dangerous master.

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Obesity and the risk of malignancy: an evolving saga

I read with interest the paper by Wilcock and Haboubi in your journal.[1]

An important related issue of huge practical importance on a day-to-day basis is the increased difficulty in making a diagnosis of cancer in obese patients.[2,3] Obesity is associated with delays to diagnosis attributed to confounding symptomatology, limitations to clinical examination and reduced image quality in most radiological examinations.

Over my 26 years in radiology I have witnessed the increasing challenges facing clinicians who are trying their best to diagnose and manage disease against an increasing prevalence of obesity. From the radiologists' perspective it appears that, regardless of the disease in question, the presentation, diagnosis and ability to deliver effective treatment without complications is impaired in obese patients. Further, outcomes for several common cancers are poorer in obese patients, in part but not exclusively due to comorbidities.[3]

There is indeed a link between obesity and increased risk of cancer, but there is also abundant observational and prima facie evidence that the diagnosis of cancer, along with many other diseases, is harder to make in obese patients, and that outcomes from treatment are poorer.

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Retrospective studies – utility and caveats

I read with interest the paper by Talari and Goyal in your journal.[1]

One substantial benefit of retrospective study designs which was not mentioned in their paper is that a retrospective design allows for the study of human decision-making without introducing the risk of bias known as the Hawthorne effect. The Hawthorne effect occurs when people behave differently because they know they are being watched.[2]

From my own experience a study of the timing of CT scanning in acute pancreatitis produced striking results.[3] The prevailing UK guideline at the time recommended that CT scanning not be performed prior to the sixth day of admission.[4] The study found that half of these patients underwent CT scanning earlier than recommended, and that none of these scans resulted in any beneficial therapeutic intervention. It is almost inconceivable that the clinicians and radiologists who requested and performed these CT scans would have deviated so hugely from the guideline had they known that they were being observed.

Much of medicine is predicated on human decision-making. Avoiding the Hawthorne effect is essential for studies of decision-making to be valid. Retrospective studies have a useful part to play in this.

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Corrigendum

Correction to An unexpected cause of chronic cough and widened mediastinum on chest radiograph

Correction to:

May Khei Hu, Patrick Liu-Shiu-Cheong, Muhammad Shakeel, Bruce Duff, David Miller, An unexpected cause of chronic cough and widened mediastinum on chest radiograph, *J R Coll Physicians Edinb* 2020; 50: 418–9

An error was made in respect of one of the co-authors' forenames: Muhammad Shakeel was previously misspelled as Muhammed Shakeel.

The authors apologise for this error.