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Letters to the editor

OVERVIEW

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COVID-19: Redeployment through the eyes of an ophthalmologist

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Editor – The COVID-19 outbreak has strained healthcare systems and resources across the world.[1] Strategies to reinforce frontline staff led to the redeployment of sub-specialty doctors.[2] Among the redeployed ophthalmologists, there was much anxiety due to publicised reports of healthcare professionals being hospitalised.[3,4] This, coupled with the prospect of being outside the realm of the eye clinic, was indeed a daunting one especially for those who had not worked on medical wards for over 10 years.

My redeployment is best summarised by a single snapshot of the monumental daily effort of the multidisciplinary team on the ward. Physiotherapists, occupational staff and nurses were thinly spread between mobilising patients, organising home support to help increase hospital capacity and keeping up with regular drug dispensing duties. Medical students were utilised on the wards as a vital extra pair of hands. Senior doctors led by example, examining patients by their bedside and astutely investigating for co-pathologies. Added to this were the frequent cameos of other specialties who promptly reviewed patients, epitomising the comradery that had brought the hospital together as one singular team.

How did I fit into this team? As an ophthalmologist, I reviewed adult and paediatric patients on the wards, ambulatory care and intensive care unit, and used this opportunity to teach junior doctors and consultants alike about ophthalmology by the bedside. My redeployed role also ranged from completing ward jobs to phoning patient families. This often meant talking to distraught family members about patients dying and relaying messages of support. Being the emotional bridge between families and patients was toilsome and often left feelings of helplessness.

COVID-19 has raised many questions on the wider socio-political preparedness, but it was also a time for individual healthcare professionals to reflect and improve. I re-evaluated my consultation style and made a conscientious effort to focus more on a patient-centred approach, even during those busy casualty clinics, and included family members in the consultations. Finally, witnessing the resilience, flexibility, bravery and altruistic behaviour of my colleagues reminded me of how proud I should be to be a healthcare professional and work in the NHS. ■

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References

1 Gandhi RT, Lynch JB, del Rio C. Mild or Moderate Covid-19. *N Engl J Med* 2020. [Epub ahead of print].
2 Academy of Medical Royal Colleges. *Plans regarding trainee redeployment during the COVID-19 pandemic A position statement from the Academy Trainee Doctors' Group*. AoMRC, 2020.
3 Iacobucci G. Covid-19: NHS bosses told to assess risk to ethnic minority staff who may be at greater risk. *BMJ* 2020;369:m1820.
4 Kirby T. Evidence mounts on the disproportionate effect of COVID-19 on ethnic minorities. *Lancet Respir Med* 2020. [Epub ahead of print].

Vitamin D binding protein in COVID-19

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Editor – With interest, we read the paper of Weir *et al* about the potential association between vitamin D deficiency and COVID-19 severity.[1] The authors focused on the regulation of Tregs and thrombotic pathways by vitamin D. However, we think that vitamin D binding protein (VDBP) may also play a role in severe pulmonary complications of COVID-19.

In patients with COVID-19 pneumonia, a hyperinflammatory syndrome with activation of the complement system may lead to acute respiratory distress syndrome (ARDS), in which the C5a–C5aR axis plays an important role. VDBP has been detected in the bronchoalveolar lavage fluid of ARDS patients. At sites of endothelial injury, VDBP-release augments the chemotactic effect of complement derived C5a and C5a des Arg, promoting monocyte and neutrophil attraction, aggregation and activation to generate an oxidative burst. By competing for the same binding site on VDBP, $25(OH)D_3$ and $1,25(OH)_2D_3$ may inhibit this chemotaxis, thereby determining disease progression and outcome.[2]

Autopsy reports from COVID-19 patients have demonstrated severe endothelial injury, widespread vascular thrombosis with microangiopathy, and significant new vessel growth in the lungs. During cell death and lung tissue injury, globular actin (G-actin) is released in the extracellular compartment and polymerises into filamentous actin (F-actin). Sera from patients with ARDS contain F-actin, which may lead to the development of microembolisms, pulmonary vascular angiopathy, and multiple organ dysfunction syndrome. SARS-CoV can induce apoptosis and actin reorganization in mammalian cells under stressed conditions.[3] Being members of the extracellular actin scavenger system, VDBP and gelsolin cleave actin and inhibit repolymerisation. However, elevated concentrations and/or prolonged exposure to VDBP-actin complexes may induce endothelial cell injury and death, particularly in the lung microvasculature.[4]

Finally, vitamin D supplementation may increase the low concentration of Tregs in COVID-19 patients.[1] Activated T cells

express CYP27B1 and can convert $25(OH)D_3$ to $1,25(OH)_2D_3$. Significant amounts of $1,25(OH)_2D_3$ can be produced locally by the involved immune cells during infection. However, VDBP controls T cell responses to vitamin D by sequestering $25(OH)D_3$ and inhibiting the production of $1,25(OH)_2D_3$ in T cells.[5]

Based on these findings, we believe that further research should also focus on VDBP in COVID-19 patients. ■

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References

1 Weir EK, Thenappan T, Bhargava M *et al*. Does vitamin D deficiency increase the severity of COVID-19? *Clin Med* 2020;20:e107–8.
2 Raymond M-A, Désormeaux A, Labelle A *et al*. Endothelial stress induces the release of vitamin D-binding protein, a novel growth factor. *Biochem Biophys Res Commun* 2005;338:1374–82.
3 Surjit M, Liu B, Jameel S *et al*. The SARS coronavirus nucleocapsid protein induces actin reorganization and apoptosis in COS-1 cells in the absence of growth factors. *Biochem J* 2004;383:13–8.
4 Ge L, Trujillo G, Miller EJ *et al*. Circulating complexes of the vitamin D binding protein with G-actin induce lung inflammation by targeting endothelial cells. *Immunobiology* 2014;219:198–207.
5 Kongsbak M, von Essen MR, Levring TB *et al*. Vitamin D-binding protein controls T cell responses to vitamin D. *BMC Immunol* 2014; 15:35.

Supplemental oxygen in COVID-19: a friend or foe?

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Editor – We read the article 'Potential role of endothelial cell surface ectopic redox complexes in COVID-19 disease pathogenesis' with great interest.[1] Dr Isabella Panfoli explains the cause of viral damage-induced microvascular inflammation and thrombosis seen in susceptible people with COVID-19. She proposes ectopic expression of electron transport chain (ETC) on the luminal endothelial cell (EC) membrane secondary to viral damage as a cause of luminal oxidative stress priming microvascular thrombosis. She comments that high oxygen input in the presence of impaired ectopic ETC can result in uncontrolled augmented reactive oxygen species (ROS) production that can be prevented by strict fine tuning of oxygen flux during mechanic ventilation. This is concordant with the experimental study by Helmerhorst *et al* who demonstrated prolonged ventilation with higher oxygen concentrations (hyperoxia) induced immune response in pulmonary compartment in mice.[2] In contrast to these, Goyal *et al* put forward that hypoxia is itself pro-inflammatory and its timely detection and correction by oxygen supplementation likely improves mortality in COVID-19 patients.[3] So, titrating fractional inspired oxygen (FiO_2) to correct hypoxia but without causing hyperoxia that could result in deleterious ROS production is of paramount importance. But which clinical criteria determines correctly the transition line between harm and therapy by supplemental oxygen? What is the correct timing? Can ROS scavengers (including N-acetyl cysteine, glutathione, alpha-lipoic acid or ascorbic acid), nuclear factor erythroid 2-related factor 2 (nrf-2) agonists, ETC complex I or III inhibitors or angiotensin-II blockers be used to liberally increase FiO_2 during mechanical ventilation? Are there other sources of ROS than ECs? It seems that we need further experimental and clinical studies to answer even the optimal dosing of supplemental oxygen in correcting hypoxaemia in patients with COVID-19. ■

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References

1 Panfoli I. Potential role of endothelial cell surface ectopic redox complexes in COVID-19 disease pathogenesis. *Clin Med* 2020; 20:e146–7.
2 Helmerhorst HJF, Schouten LRA, Wagenaar GTM *et al*. Hyperoxia provokes a time-and dose-dependent inflammatory response in mechanically ventilated mice, irrespective of tidal volumes. *Intensive Care Med Exp* 2017;5:27.
3 Goyal DK, Mansab F, Iqbal A, Bhatti S. Early intervention likely improves mortality in COVID-19 infection. *Clin Med* 2020;20: 248–50.

Challenges to new doctors during the pandemic

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Editor – Thank you for publishing the article 'FiY101: A guide for newly qualified doctors'.[1] It offers a practical approach to managing common queries and anxieties for new doctors. As a trainee working through the COVID-19 pandemic from its start, I have observed and experienced a number of challenges to ways in which we work and to our wellbeing that are relevant to newly qualified doctors. I wish to highlight a few of these alongside the helpful advice already given.

The authors rightly mention that foundation rotas are subject to change. During the pandemic, not only have rota patterns changed but a number of doctors have been redeployed to entirely different departments.[2] Often those redeployed first have been foundation doctors who had to readjust not only to a new rota but also to a new team and have had to cover patients with completely different problems at short notice – as in the case of doctors redeployed from surgical to medical jobs.

New doctors should also bear in mind the need to prioritise booking annual leave early. It is often difficult to coordinate leave with other members of the team, on-call commitments and social events.[3] There may be a temptation to delay booking leave until lockdown restrictions have been sufficiently lifted, allowing safe international travel and gathering in large groups at events. However, I would advise, based on my experience, that it would be more prudent to book leave even in the absence of definite social plans as many of us have found that we needed the time away from work simply to rest and recover.