occupies the centre of the MS plaque.[3] 7 Tesla MRI of the brain demonstrates the presence of a central vessel in 87% of visible white matter lesions called the 'central vein sign'.[4] ■

SHAHID A KAUSAR
Consultant physician in stroke, geriatrics and general medicine, Russells Hall Hospital, Dudley, UK

References

1 Ford H. Clinical presentation and diagnosis of multiple sclerosis. *Clin Med* 2020;20:380–3.
2 Kostulas N, Larsson M, Kall TB, von Euler M, Nathanson D. Safety of thrombolysis in stroke mimics: an observational cohort study from an urban teaching hospital in Sweden. *BMJ Open* 2017;7: e016311.
3 Tan IL, van Schijndel RA, Pouwels PJ *et al*. MR venography of multiple sclerosis. *AJNR Am J Neuroradiol* 2000;21:1039–42.
4 Tallantyre EC, Morgan PS, Dixon JE *et al*. A comparison of 3T and 7T in the detection of small parenchymal veins within MS lesions. *Invest Radiol* 2009;44:491–4.

Adrenal insufficiency and checkpoint inhibitors for cancer

DOI: 10.7861/clinmed.Let.20.5.8

Editor – Simpson *et al* provide a welcome overview of the importance of the recognition and treatment of adrenal insufficiency.[1] However, there is no mention of checkpoint inhibitors for cancer, which have emerged as an important and common cause of secondary adrenal insufficiency, and rarely primary adrenal insufficiency.[2] The importance and challenge of prompt recognition has been recognised.[3] Checkpoint inhibitors are approved globally for the treatment of multiple different cancer types, including non-small-cell lung carcinoma, melanoma, bladder, kidney, and head and neck cancers. Given that around 10% of patients treated with ipilimumab, and 1–2% of patients treated with PD-1/PD-l1 inhibitors develop adrenocorticotropic hormone (ACTH) deficiency, we propose that all patients with current or recent checkpoint inhibitor use should be included in those considered at risk of an adrenal crisis.

In addition, a third of patients receiving a checkpoint inhibitors will require high does corticosteroids for management of one or more immune related adverse events and it is vital that oncological practice takes on the need to issue these patients with the new steroid card and appropriate education.[4,5] ■

DANIEL L MORGANSTEIN
Consultant endocrinologist, Chelsea and Westminster Hospital NHS Foundation Trust and The Royal Marsden NHS Foundation Trust, London, UK

JAMES LARKIN
Consultant medical oncologist, The Royal Marsden NHS Foundation Trust, London, UK

References

1 Simpson H, Tomlinson J, Wass J *et al*. Guidance for the prevention and emergency management of adult patients with adrenal insufficiency. *Clin Med* 2020;20;371–8.
2 Nogueira E, Newsom-Davis T, Morganstein DL. Immunotherapy-induced endocrinopathies: assessment, management and monitoring. *Ther Adv Endocrinol Metab* 2019;10:2042018819896182.
3 Higham CE, Olsson-Brown A, Carroll P *et al*. Society for Endocrinology endocrine emergency guidance: Acute management of the endocrine complications of checkpoint inhibitor therapy. *Endocrine Connections* 2018;7:G1–7.
4 Agarwal K, Yousaf N, Morganstein D. Glucocorticoid use and complications following immune checkpoint inhibitor use in melanoma. *Clin Med* 2020;20:163–8.
5 Horvat TZ, Adel NG, Dang T-O *et al*. Immune-related adverse events, need for systemic immunosuppression, and effects on survival and time to treatment failure in patients with melanoma treated with ipilimumab at Memorial Sloan Kettering Cancer Center. *J Clin Oncol* 2015;33:3193–8.

A Bayesian strategy for the asymptomatic healthcare worker

DOI: 10.7861/clinmed.Let.20.5.9

Editor – The mean corpuscular volume, age, platelets and eosinophils (MAPE) strategy proposed by the Formica *et al* might help to resolve the conundrum of the false negative reverse transcriptase polymerase chain reaction-based test (so-called antigen test) for SARS-CoV-2 and the transiently negative antigen test for that infection (ie COVID-19) in some healthcare workers.[1–4] The conundrum can only be resolved by a Bayesian diagnostic strategy.

The conundrum is compounded by the phenomenon of the transiently negative antigen test.[3] This phenomenon was elucidated by Kucirka *et al* who showed that over a 4-day period before the onset of symptoms, the probability of a false negative antigen test result in an infected person decreases from 100% to 67% on day 4. On the day of symptom onset, the median false negative rate can be as high as 38% (95% confidence interval (CI) 18–65%). This decreases to 20% (95% CI 12–30%) 3 days after symptom onset.[3]

Accordingly, when routine testing is undertaken among healthcare workers, a complementary strategy would be an evaluation of C-reactive protein (CRP) as well as MAPE. In one retrospective study, a high-sensitivity CRP level equal to or greater than 4 mg/L was present in 95.0%, 52.2%, 74.7% and 86.7% of COVID-19 patients as opposed to 87.2%, 28.8%, 31.3% and 45.2% of controls, respectively. The sensitivity of CRP was improved by using that parameter in combination with eosinopenia. The combination of eosinopenia and elevated CRP yielded a sensitivity of 67.9% and a specificity of 78.2% for the diagnosis of COVID-19 infection. The area under the curve amounted to 0.730.[5]

Given that in a retrospective study of 27 COVID-19 patients, the size of the lung lesions detected by computed tomography (CT) of the chest also showed a correlation with CRP, the detection rate of infected persons with falsely negative antigen tests might, arguably, be further improved by the combined strategy of evaluation of MAPE (which includes eosinopenia), CRP and CT of the chest; the latter utilised only in those subjects with high CRP.[6] The combination of MAPE, raised CRP, and CT-identifiable lung pathology would powerfully enhance the pre-test probability of COVID-19 infection. The deciding factor for triage of healthcare workers with a negative test result would be the weight of pre-test probability. ■

OSCAR JOLOBE
Manchester Medical Society, Manchester, UK

References

1 Formica V, Minieri M, Bernardini S *et al*. Complete blood count might help to identify subjects with high probability of testing positive to SARS-CoV-2. *Clin Med* 2020;20:e114–9.
2 Woloshin S, Patel N, Kesselheim AS. False negative tests for SARS-CoV-2 infection. Challenges and Implications. *N Engl J Med* 2020;383:e38.
3 Kucirka LM, Lauer SA, Laeyendecker O. Variation in false-negative rate of reverse transciptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. *Ann Intern Med* 2020:M20-1495. [Epub ahead of print].
4 Arons MM, Hatfield KM, Reddy SC *et al*. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *N Engl J Med* 2020;382:2081–90.
5 Li Q, Ding X, Xia G *et al*. Eosinopenia and elevated C-reactive protein facilitate triage of COVID-19 patients in fever clinic: A retrospective case-control study. *EClinicalMedicine* 2020;3:100375.
6 Wang L. C-reactive protein levels in the early stage of COVID-19. *Med Mal Infect* 2020;50:332–4.

COVID-19 viral expulsion through chest drains

DOI: 10.7861/clinmed.Let.20.5.10

Editor – We thank Akhtar *et al* for their very timely article on aerosol dissemination through a pleural drain bottle.[1] We completely agree with their conclusion that further work in this field is required and would like to point out complementary work by Duffy *et al* which showed that aerosol emissions increased with increased air flow, with the largest increase observed in smaller particles (0.3–3 microns).[2] A bubbling chest drain thus generates aerosols and a viral filter reduces the aerosols. Pleural fluid has been shown to be positive for SARS-CoV-2 in a post-mortem series and data are lacking from the cases but it seems effusions developed due to other causes rather than the viral infection.[3] The above evidence is currently reflected in the British Thoracic Society that bubbling drains in patients should have droplet exposure minimised by connecting any chest drain to wall suction to create a closed system, applying the described filter or using a digital suction device.[4] The Acute Care Surgery and Critical Care Committees have produced a clear algorithm for chest drain insertion and there is now enough evidence for this to be widely implemented.[5] Locally, this has been adopted with the emergency team only performing chest drains in the department for emergency cases (trauma or tension pneumothorax) and that patients are being moved to a respiratory ward to wait for their SARS-CoV-2 swab to be available before a chest drain is performed. Our current time for a swab is approximately 4 hours (45 minutes for a fast-track swab) and so far, there has been no excess mortality or morbidity to waiting for a swab result. We have plans in place to perform therapeutic aspirations if a procedure is required for symptom relief if the patient cannot wait. ■

AVINASH AUJAYEB
Consultant in respiratory and acute medicine, Northumbria Healthcare NHS Foundation Trust, Cramlington, UK

References

1 Akhtar MR, Ricketts W, Fotheringham T. Use of an antiviral filter attached to a pleural drain bottle to prevent aerosol contamination with SARS-CoV-2. *Clin Med* 2020;20:e60–1.
2 Duffy C, Kidd A, Francis S *et al*. Chest drain aerosol generation in covid-19 and emission reduction using a simple anti-viral filter *MedRxiv* 2020.07.13.20152264.
3 Schaller T, Hirschbühl K, Burkhardt K *et al*. Postmortem examination of patients with COVID-19. *JAMA* 2020;323:2518–20.
4 Hallifax R, Wrightson J, Bibby A *et al*. *Pleural services during the COVID-19 pandemic*. British Thoracic Society, 2020. www.brit-thoracic.org.uk/documentlibrary/quality-improvement/covid-19/pleural-services-during-covid-19-pandemic
5 Pieracci FM, Burlew CC, Spain D *et al*. Tube thoracostomy during the COVID-19 pandemic: guidance and recommendations from the AAST Acute Care Surgery and Critical Care Committees. *Trauma Surg Acute Care Open* 2020;5:e000498.