

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 ■

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Adrenal insufficiency and checkpoint inhibitors for cancer

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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 dose 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} ■

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A Bayesian strategy for the asymptomatic healthcare worker

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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. ■

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