Letters to the editor

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End-tidal carbon dioxide as a screening tool in excluding pulmonary embolism

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Editor – In our 2014 article, we demonstrated that end-tidal carbon dioxide (ETCO₂; the level of carbon dioxide that is released at the end of an exhaled breath) is a reliable screening test to rule out pulmonary embolism.¹ There were a small number of patients (n=100), with only 38 patients with pulmonary emboli (PEs). We demonstrated then that an ETCO₂ of <4.3 kPa (32.3 mmHg) had a sensitivity of 100%, specificity of 65% and negative predictive value (NPV) of 100%.¹

In view of the small number, we elected to extend the study to 200 cases and repeat the analysis on 70 patients who had PEs on computed tomography (CT; Fig 1).

Our updated results show similar statistics with an excellent NPV in ruling out PEs (Table 1). Our institution administers over 1,000 CT pulmonary angiographies (CTPAs) per year, reducing these can have a huge financial saving locally and to the NHS at large, as well as reducing the number of complications from procedures due to allergies or kidney problems relating to the dye used for CTPAs. ETCO₂ can be applied in the emergency rooms and medical assessment wards. This helps with the flow of cases as well without the need for venipuncture.

Table 1. End-tidal carbon dioxide classification table over a range of cut-off thresholds

<table>
<thead>
<tr>
<th>ETCO₂, kPa</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Positive predictive value, %</th>
<th>Negative predictive value, %</th>
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<td>9</td>
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</table>

ETCO₂ = end-tidal carbon dioxide.

Fig 1. Computed tomography pulmonary angiography (CTPA) positive and CTPA negative results for end-tidal carbon dioxide (ETCO₂). The red line represents threshold of 4.3 kPa (32.3 mmHg). This figure shows that no patient with a ETCO₂ of >4.3 kPa had a pulmonary embolism. PE = pulmonary embolism.

Fig 2. Area under receiver operator characteristic curves (AUROCCs) for the true positive rate against the false positive rate for different possible cut-off points. a) Wells score, AUROCC = 0.5391. b) D-dimer, AUROCC = 0.8468. c) End-tidal carbon dioxide, AUROCC = 0.8768.
This is the only study to compare ETCO$_2$ with D-dimer; D-dimer is the gold standard to rule out PE at present (Fig 2). Both parameters look at similar tests but from different perspectives. D-dimer measures the clot lysis (fibrinolysis) and ETCO$_2$ looks at the physiological consequences of the clot, ie dead space ventilation caused by the clot in the pulmonary circulation. We will probably require a larger sample size for more definitive conclusions, but this is a promising step in the right direction.

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The potential threat of Nipah virus

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Editor – I read with interest the review article by Dr Alam that discusses the potential future threat from Nipah virus (NiV). Since first being isolated in 1999 in Malaysia, it has caused further outbreaks of encephalitis in south and east Asia, most recently in India in 2021, thus posing an ongoing threat. The review also importantly discusses the fact that human-to-human transmission of NiV has been observed and that it may have pandemic potential. The fact that NiV is in the World Health Organization (WHO) Research and Development (R&D) Blueprint list of epidemic threats requiring urgent R&D action highlights the global concern regarding NiV. Despite the high mortality from NiV infection ranging from 40% to 91%, Dr Alam also emphasises that there are no licensed treatments, with care being only supportive. Lessons must be learnt from our experiences with the COVID-19 pandemic as well as the ongoing multi-country monkeypox outbreak. Greater efforts must be made to optimise our preparedness for future potential threats (such as NiV) and take advantage of any opportunities that may facilitate this preparedness; for example, regarding antiviral therapy for NiV infection, a study was conducted in which African green monkeys were challenged with a lethal dose of NiV (Bangladesh genotype): all animals who received remdesivir survived whereas all the control animals died. Remdesivir has been used widely during the COVID-19 pandemic and continues to feature in current national COVID-19 treatment guidelines. We should, therefore, utilise our vast experience with the use of this antiviral to study its potential role in the treatment of human NiV infection. In macaques, remdesivir penetrates poorly into the central nervous system (CNS) with a brain-plasma ratio of <0.05. However, its CNS penetration in humans is largely unknown but is of interest not only because NiV frequently causes an encephalitis but also in view of the fact that there have been numerous reports of COVID-19-associated encephalitis. Many patients with COVID-19-associated neurological disease receive remdesivir that potentially provides an opportunity to study its blood-brain barrier penetration and/or characterise the effects of remdesivir on brain tissue through post-mortem studies, indirectly providing valuable information regarding its possible utility in the treatment of CNS disease caused by NiV.

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References