A fresh look at D-dimer in suspected pulmonary embolism

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Newer imaging approaches in suspected pulmonary embolism (PE) such as the PISA-PED perfusion lung scanning criteria,[1] spiral computed tomography,[2] and leg vein ultrasound[3] are attracting widespread interest. Attempts are being made to clarify and rationalise clinical diagnosis,[4] and the use of low molecular weight heparin in PE[5] is increasing. However, it is often forgotten that clinical suspicion of PE turns out to be incorrect in five out of every six patients properly investigated.[6 7] Since in most district general hospitals imaging tests for suspected PE cannot usually be arranged immediately, such patients have to be admitted and heparin started while awaiting an isotope lung scan which often fails to give an unequivocal answer. All this is costly in time and resources and engenders considerable anxiety in the patient.

A simple cheap and accurate test to exclude PE that is also available out of hours would be of great interest to general physicians. Hopes for plasma D-dimer seemed not to have been fulfilled because none of the rapid latex tests is sufficiently accurate, whereas the ELISA "gold standard" is complex and takes several hours. For these reasons the recent British Thoracic Society review of PE[4] excluded D-dimer from its diagnostic algorithm. The paper from New Zealand by Egermayer *et al* in this issue of *Thorax*[8] suggests that this should be reconsidered. Their study is of particular interest because it comes, not from a dedicated thrombosis research unit, but from a large hospital setting familiar to most British general physicians. This explains why, as is still worryingly common,[9] almost half their colleagues' patients treated for PE had been inadequately investigated. However, of those that were, PE was excluded in 83%, as above. Of particular significance was the finding that D-dimer was negative in only 6.5% of those where PE was either proved directly (two of 40 patients) or indirectly (three of 37 patients). Their results also suggested that half the lung scans requested might have been avoided.

The commercial kit they used, known as SimpliRED D-dimer (SRDD), costs less than £4 per assay. It is detected by an antibody reaction causing agglutination of the patient's own red cells using whole blood so that centrifugation is not necessary, an advantage over latex assays. The result is read at two minutes. However, although hailed as a bedside test, accurate volume measurement and timing are important and the inexperienced could misread a weak positive result. Hence Egermayer *et al* sent their specimens to the laboratory where they could readily be analysed by on call pathology technicians—that is, a "real time" rather than "near patient" test.

Although the SRDD test was first reported eight years ago,[10] until recently publications on its use were confined to specialist journals, most concentrating on its place in excluding deep vein thrombosis (DVT). As well as the five papers quoted, four newer studies[11–14] confirm that a negative SRDD result is found in less than 5% of patients with proven DVT, usually those with distal clot only. A tenth study[15] is the exception in that the SRDD test failed to detect DVT in eight of 19 patients, but numbers were small and the test was performed at the bedside by a physician rather than a trained laboratory technician.

Although there is less information in PE, two published pilot studies from highly respected units[16 17] found that the SRDD test was negative in only one of 35 patients with proven PE. Along with the current report, the false negative rate in PE appears be the same as for DVT (3–5%). Indeed, results (in abstract form) from a much larger cohort—1018 patients of whom 187 had PE—confirm a negative predictive value of 97%.[7] In the PIOPED study[18] PE was present in 4% of those with a normal ventilation-perfusion (V/Q) lung scan as well as those with low clinical and scan probability. Since clinicians are prepared to withhold anticoagulation in such patients, can a similar strategy be adopted in those with suspected PE and negative SRDD?

In patients with a low clinical probability of DVT which, as in PE, applies to most of those investigated, there is now sufficient evidence that a negative SRDD result excludes the diagnosis without leg imaging being necessary. Provisional results from the recent Canadian DVT study, where again thromboembolism was absent in five in six of the study population, imply that 41% (207/496) of such tests could have been avoided.[14] In their large parallel PE study[7] a false negative SRRD result was found in only four (1%) of 448 patients with low clinical probability. This seems an acceptable error rate with 44% of their patients needing no direct or indirect imaging.

Following four years' experience in DVT, low molecular weight heparin has become an accepted treatment in PE. Likewise, the promise of this cheap simple and rapid blood test, already fulfilled in DVT, is likely to extend to PE, potentially leading to major changes in clinical practice and use of resources.

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