differently in pregnant women with suspected pulmonary embolism than in non-pregnant patients owing to (1) the lower prevalence of pulmonary embolism in pregnant women with suspected pulmonary embolism than in non-pregnant women with suspected pulmonary embolism, and (2) the acknowledged differences in D-dimer concentrations in normal pregnancy compared with the non-pregnant population. Furthermore, measurements of D-dimer concentrations must always be combined with validated tests to assign a low or moderate pretest probability to safely exclude pulmonary embolism without imaging, and these tests do not exist in pregnancy.

We agree with Chirag Patel and colleagues that chest radiography is an essential part of the work-up of patients with suspected pulmonary embolism in that it helps exclude alternative diagnoses that may preclude further imaging. Our paper not only discussed the usefulness of ventilation/perfusion (V/Q) scintigraphy for suspected pulmonary embolism in pregnancy, highlighting the advantages of V/Q scans outlined by Patel and colleagues, it discussed potential limitations of such an approach in pregnant women, including a likely lower positive-predictive value than in the non-pregnant population and failure to offer an alternative diagnosis.

Although computed tomographic pulmonary angiography (CTPA) is subject to limitations related to the physiological increase in plasma volume, cardiac output, and heart rate in pregnancy, the cited rate of non-diagnostic scans of 35.7% is higher than rates reported in published studies and likely to be related to the imaging protocol. Indeed, a case-control study of consecutive pregnant patients imaged by use of a reduced-dose protocol reported no significant differences between pregnant and non-pregnant controls in quantitative measurements of vascular enhancement in the segmental and subsegmental arteries. Specific CT protocol modifications are probably required in pulmonary embolism imaging in pregnant patients to optimise diagnostic yield.

We agree with Catherine Deneux-Tharaux and colleagues that maternal mortality from pulmonary embolism seems to be on a downward trend in the developed world. However, reports from non-European countries still list this disease as a leading cause of mortality. Pulmonary embolism remains an important cause of maternal mortality, and the prevention, diagnosis, and management of this disease in this population remains an important challenge.

We declare that we have no conflicts of interest.

Ghada Bourjeily, Hanan Khalil, Marc Rodger
GBourjeily@wihri.org

Department of Medicine (GB) and Department of Diagnostic Imaging (MB), Warren Alpert Medical School of Brown University, Women and Infants Hospital of Rhode Island, Providence, RI 02903, USA; and Department of Medicine, Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada (MR)


Future diagnosis of sepsis

The Prove-it sepsis assay, assessed by Päivi Tissari and colleagues (Jan 16, p 224), adds a new technique to the array of molecular methods available for rapid identification of microorganisms in growth-positive blood cultures. The clinical value of rapid identification, however, almost fully depends on the clinical usefulness of the blood culture.

The total turnaround time of blood culture and molecular identification could still be too long. Indeed, empirical antimicrobial therapy is usually started at the time of phlebotomy and may already have been modified in patients with clinical deterioration before notification of growth in blood cultures. Additionally, only a minority of patients with sepsis have positive blood cultures, and some blood cultures may read false-negative owing to previous use of antibiotics. Therefore it is questionable whether assays for rapid identification of micro-organisms in blood cultures will contribute significantly to antimicrobial management and be so cost-effective as to warrant routine implementation.

A real advantage in diagnosis of sepsis will be obtained by direct detection of microbial DNA in blood: results are available within a few hours and are presumably unaffected by antibiotics. Additionally, the amount of microbial DNA can be quantified. At present, low sensitivity and lack of an adequate gold standard are the main limitations for widespread application of such direct techniques, but there are promising developments.

Altogether, we think that assays for faster identification of microorganisms in blood cultures only form an intermediate stage and that future diagnostic tests for sepsis will evolve towards detection of microbial DNA directly in blood.

We declare that we have no conflicts of interest.

Remco P H Peters, Paul H M Savelkoul, Christina M J E Vandenbroucke-Grauls rph.peters@gmail.com

VU University Medical Center, Department of Medical Microbiology and Infection Control, Amsterdam, Netherlands (RPHP, PHMMS, CMEVFG); and ANOVA Health Institute, Khuţo Khuţula, PO Box 2243, 0850 Tzaneen, South Africa (RPHP)

Paivi Tissari and colleagues1 present accurate and rapid identification of bacterial species from positive blood cultures with a DNA-based microarray platform (the Prove-it sepsis assay). This assay yielded a clinical sensitivity of 94·7% (95% CI 93·6–95·7) and specificity of 98·8% (98·1–99·2). However, the sensitivity and specificity were calculated with the combined data for all pathogens, not for each pathogen individually, and could be confusing for readers. For example, if a sample is diagnosed as Escherichia coli by blood culture analysis and as Staphylococcus epidermidis by the Prove-it assay, the real diagnosis should be E coli (false positivity for S epidermidis); however, it would be S epidermidis in Tissari and colleagues’ study. Therefore, the sensitivity and specificity of the Prove-it sepsis assay should be reconsidered.

With its flexible design and persistent modification for difficulties related to PCR multiplexing capacity in polymicrobial bacteraemia, the Prove-it sepsis assay represents an advance in clinical diagnosis. However, further study with strict statistical analysis is needed before its widespread application.

We declare that we have no conflicts of interests.

Juan Chen, *Youxin Wang, Wei Wang sdwangyouxin@163.com

Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China (JC); School of Public Health and Family Medicine, Capital Medical University, Beijing 100069, China (YW); and Graduate School, Chinese Academy of Sciences, Beijing, China (WW)


Authors’ reply

Although Remco Peters and colleagues correctly state that our total diagnostic turnaround time of blood culture and molecular identification may still be too long, we are less optimistic than they are about the next step of accurate and direct detection of microbial DNA in blood.

One of us has shown that such necessary detection of perhaps only a few bacterial genome copies per mL of blood remains a difficult balance between sensitivity and specificity.1 These so-called ultrasensitive methods are technically difficult and merely detect microbial “DNA-aemia”. This DNA might originate from pathogens already killed by antibiotics, possibly offering an advantage over culture-dependent systems in view of their proinflammatory role via TLR9,2 but might also represent fragments whose origin is far from clear. The clinical significance of such fragments to sepsis is far from established. Microbial growth is a natural, cheap PCR and in our hands yields high diagnostic performance, admittedly at some time cost. Perhaps the solution is a combination of test technologies to suit individual clinical priority.

Juan Chen and colleagues correctly state that the ideal way to assess sensitivity and specificity is to make such calculations for each pathogen separately. To do so would require a far larger dataset—perhaps 50 times as large as our study’s, which is already far the largest in this field. Although such a large and perhaps otiose study is awaited, we stand by our results, especially those relating to the most relevant and abundant species.

The message we continue to wish to convey is that, after perhaps 15 years of development of PCR technology in this specialty, we believe this platform to be the first that delivers robust, consistent, and accurate results, and furthermore (if front-end extraction is taken out of the equation) can be done with a few hours’ training and with nothing more than a laptop computer whose USB port powers the relatively cheap reader.

We declare that we have no conflicts of interest.

*Vanya Gant, Martti Vaara, Minna Makki, Alimuuddin Zumila, Jim Huggett

vanya.gant@uclh.nhs.uk

University College London Hospitals NHS Foundation Trust, London W1T 4JF, UK (VG, AZ, JH); Division of Clinical Microbiology, Helsinki University Hospital Laboratory, Helsinki, Finland (MV); and Mobidiag, Helsinki, Finland (MM)


Genes and stress cause coronary atherosclerosis not saturated fat

The “unequivocal evidence” that atherosclerosis in Egyptian mummies “almost certainly” resulted from a “diet rich in saturated fat” (Feb 27, p 178)1 is pure speculation. This fallacious proposal was popularised by Ancel Keys,2 who noted a correlation between saturated fat intake, elevated cholesterol concentrations, and increased heart attacks, and has been perpetuated by the cholesterol cartel of manufacturers of statins and low-fat foods. Although data were available from 22 countries, Keys selected only seven to prove his theory. Had he included all countries, the results would have been very different. Indeed, figures from five others would have led him to conclude that the more saturated fat consumed, the lower the incidence of coronary mortality.

Large epidemiological studies such as Framingham and MRFIT failed to confirm Keys’ findings, and more recently, MONICA,3 which assessed